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ENVIRONMENTAL PROTECTION AGENCY

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This report is a compilation of papers,presented over a 3-day period,on the subject of the substitute chemicals program. Papers deal with such related areas as: purpose, organization, and operation of the substitute chemicals program; initial scientific, mini-economic, biosphere, and socioeconomic reviews; progress in EPA research - new directions and overview; worldwide pesticide research and perspectives; WHO in pesticide research, as well as food and agriculture organization; U.S. participation in Codex; prerequisite conditions for determination and efficient realization of substitute chem. program in some European and developing countries; EPA's pesticide monitoring program; research in USDI; nonagricultural use pesticides; future of pesticide research; overview of ecological effects; terrestrial effects,and marine life,and fresh water effects; preliminary systems analysis as a tool for research program design; intra-and extramural health effects research and long-range health effects.

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August 14 - 16, 1974

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First Day

FUNCTIONS AND OVERVIEW OF THE OFFICE OF PESTICIDE PROGRAMS: HIGHLIGHTS OF OPP PROGRAMS

Henry J. Korp, L. L. D. *

I am most pleased to see you all and to have the opportunity of welcoming you to our conference on the Alternative Chemicals Program. I am delighted with the fine national and international representation we have here today — surely there are no significant aspects of pesticides research activities which are unfamiliar to this gathering. The diversity of expertise and backgrounds in this room is most impressive, and on behalf of EPA, I say thanks to each of you for your interest and participation in what we feel will be a very informative and productive session for us all.

It's good to see many of my old friends here today, and also to see many whom I had the pleasure to meet for the first time last night and this morning. To those of you I am meeting for the first time, I'd like to introduce to you the basic functions of the Office of Pesticide Programs and to explain our overall attitude toward the regulation of pesticide chemicals.

Certainly the amendments to the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) passed by the Congress 2 years ago this October have to a great extent defined our direction and objectives. I think it is most helpful to keep in mind the reasons the FIFRA amendments were initiated in the first place. The House Agriculture Committee, which, as you know, designed the amended legislation, described the reasoning behind the legislation in the following manner.

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*Deputy Assistant Administrator for Pesticide Programs, U.S. Environmental Protection Agency

> . . . the Committee found the greatest need for revision of existing laws to be in the area of strengthening regulatory control on the uses and users of pesticides; speeding up procedures for barring pesticides found to be undesirable; streamlining procedures for making valuable new measures, procedures, and materials broadly available, strengthening enforcement procedures to protect against misuse of these biologically effective materials; and creating an administrative and legal framework under which continued research can produce more knowledge about pesticides as well as developing alternative materials and methods of pest control . . . old FIFRA is changed from a labeling to a regulatory program.

The FIFRA amendments, if I may oversimplify, reflect the recognition of an important concept — that as our knowledge about pesticides and their fate in the environment has increased, so has our need to possess the administrative tools to effect regulation of these substances commensurate with this ever-increasing degree of scientific expertise. Amended FIFRA provides us with the flexibility to respond to a dynamic situation. The more we discover, the better we can understand the priorities of environmental quality, and the better we can discern and avoid, to use a phrase oft employed in the FIFRA amendments, "unacceptable hazards to man and the environment."

Often, when I explain the function of the Office of Pesticide Programs, I discuss with my listeners a long established precept of our Agency: That our job is to ensure that the benefits of the use of any given registered pesticide outweigh the risks which could accompany such use. If I'm lucky, no one asks me exactly how we accomplish this evaluation! Certainly, there are no magic formulas for weighing the benefits and risks of a pesticide's use and for reducing a myriad of data to a single infallible truth. We all know that there is a certain inherent risk in the use of any pest control chemical. This fact is recognized in every registration action, and is recognized in our continuing post-registration reviews. We don't cancel a product's registration simply on the basis that a risk is posed by its continued use.

If there is reason to believe that the risk is greater than was anticipated at registration, though, we are most concerned and conduct a thorough evaluation of the situation, we ask ourselves about the ways that these risks can be reduced and the extent to which they can be reduced. How far can labeling go toward this end? Or other restrictions — use restrictions (as will be provided by our regulations implementing section 3 of the amended Act), geographic area restrictions, integrated management program restrictions, packaging restrictions, formulation variables, and so on? The new Act unquestionably provides us with a great deal of flexibility in taking action short of cancellation. And on the benefit side — how crucial is the use? Is it necessary to Public Health Programs or a major food source, or is it directed toward a nuisance or inconvenience? These, among many other significant factors, are the questions we must ask ourselves in assessing the continued use of pesticide products. And another factor is important too, of course, which is the reason we're together here today: What alternatives does society have to the pesticide in question? Are these alternatives more or less acceptable from the standpoint of human health and environmental well-being in general? These are questions of crucial import, and we will quite obviously discuss these issues in depth as this conference progresses.

These are some of our fundamental considerations in pesticides regulation, and our Office of Pesticide Programs is naturally concerned in an overall way with meeting the challenges of the complex decisions-making progress in this important area. As promised, though, I'd like to explain briefly more about the organization of OPP, and the various functions exercised by our four divisions: Registration, Operations, Technical Services, and Criteria and Evaluation. Those familiar bear with me.

The Registration Division is headed by Mr. John B. Ritch, Jr., as Director. As our friends in industry know well, the two primary functions of this Division are to register individual pesticide products and to establish residue tolerances. The Division reviews the data submitted by an applicant to ensure that all the criteria for registration are met before an EPA number is assigned.

The Registration Division has a tremendous job ahead in the next 2 years. There are approximately 34,000 products currently registered which must be re-registered under section 3 of the amended FIFRA and classified for general or restricted use. In addition, approximately 15,000 intrastate products must be classified and registered. All of this, of course, is in addition to the normal workload of the Division, which conducts around 15,000 actions a year.

Our Operations Division is headed by Dr. John V. Osmun, and is responsible for the development of programs to enhance the effectiveness of Governmental activities in the pesticide area. This Division provides program policy direction to technical assistance and training programs. Operations was responsible, for example, for EPA's part in Project Safeguard, which was a program conducted last year in the South to train applicators in the use of parathion and other highly toxic organophosphates. Operations also develops and recommends program content and model legislation for states and, through the Regional Offices, assists states in developing and improving their individual programs. This Division also participates in Federal interagency activities in the pesticide area and coordinates information on pesticide accidents and incidents.

One of the biggest jobs undertaken by Operations has been the development of the regulations to implement section 4 of the amended Act, which concerns the certification of pesticide applicators to employ restricted use pesticides. Defining the procedures for certification has been a complex task, and we have solicited comments from the pesticide industry, farm oriented associations, and other interested parties in writing these difficult regulations, which we hope to publish as final very shortly. Operations is, of course, also working very closely with the states in developing plans to conduct the actual certification of pesticide applicators. As most of you know, I am sure, our goal is to have all those who so desire, to be certified to use restricted pesticides by October 1976.

Our Technical Services Division, whose Director is Dr. William S. Murray, is responsible for the performance of laboratory investigations needed by OPP. The Division conducts epidemiological studies of various exposed population groups and seeks information on the potential effects of these exposures on the induction of harmful health effects. Technical Services has the responsibility for operating, planning, designing, and interpreting data collected in the National Pesticide Monitoring System, which includes operating and coordinating responsibility for monitoring pesticide residue levels in air, water, soil, crops, livestock and aquatic and land animals. Another of its primary functions is in the Systems and Information side of our program, which includes the development, operation, and maintenance of data storage and retrieval systems in OPP, and publishing of two periodicals, the Pesticides Monitoring Journal and the Health Aspects of Pesticides Abstract Bulletin. Technical Services also prepares the "Compendium of Registered Pesticides," which is familiar to many of you.

I know I don't have to introduce the Director of the Criteria and Evaluation Division, Dr. Leonard Axelrod, to you, since he has arranged this conference and invited you here. Criteria and Evaluation is responsible for the establishment of standards and criteria to be applied in the setting of tolerances and environmental, human safety, and efficacy standards applicable to the registration of pesticide products. One of its primary functions is to review currently registered pesticide chemicals and recommend to me appropriate regulatory actions as indicated by its findings. The reviews include the assessment of environmental, human and wildlife safety, economic aspects, and all other pertinent ingredients in the risk-benefit analysis. And, of course, the Alternative Chemicals Program is part of this responsibility. The Criteria and Evaluation Division also provides technical support to the Office of Enforcement and General Counsel necessary to the conduct of administrative hearings and regulatory actions. Appropriate guidelines, standards and criteria needed by other components of EPA and other governmental agencies are developed, based on a comprehensive assessment of pesticides and their impact on the environment. Research needs for OPP are developed and transmitted to the Office of Research and Development, and monitoring requirements for pesticides are developed and program policy direction to monitoring activities is provided. C&E is also responsible for the major preparation of the "Guidelines for Registering Pesticides in the United States," which we anticipate will be a great help to applicants; this document explains in detail the type of information needed to obtain registration. We expect to have the "Guidelines" published by October of this year.

As far as our goals are concerned, we have four major strategies which we hope to accomplish in the coming years.

1. First, and most obvious, is to promulgate the regulations necessary to fully implement the FIFRA amendments. This task must be completed by October 1976.

2. Secondly, we desire to reduce adverse health and environmental effects from the use of pesticides. We anticipate accomplishing this goal through the certification of applicators, improved labeling and packaging of pesticide products, timely enforcement against misuse, public education programs, and whatever other regulatory actions we discern are needed.

3. Thirdly, we intend to establish a better comprehensive hazard evaluation system to better understand the nature and extent of adverse effects of pesticides on man and the environment.

4. And, of course, our other goal is to assess the technological, economic, social, and physical environments related to pesticide use and to determine the

changes occurring to operating environments. Principal near-term research emphasis will be place on:

- Generating data to support current and anticipated litigation
- Devising standardized laboratory test methodologies
- Developing model ecosystems
- Exploring alternative pesticide possibilities

Before closing, I would like to emphasize that we are here today to share our thoughts and intentions with you and to explain expressly our plans and the reasons behind them. The Office of Pesticide Programs is most concerned to conduct its business with the maximum of openness in all aspects of our program development. We have no intention of secretly devising any great schemes which we can suddenly thrust on the unsuspecting public. On the contrary, we welcome, we solicit, the comments and advice of all who will be affected by our regulatory activities. This conference will be a magnificent opportunity for us to explain our policies and to clear up or avoid any misunderstandings or apprehensions which you may have. We desire to put this Alternative Chemicals Program in perspective, to discuss how it fits into our research and program objectives as a whole, and to find out your feelings and opinions on the issues. In short, we want this conference to be a sharing of information and thoughts. I very sincerely thank all of you for participating in this sharing process. I know that together we can make great progress in contributing to a finer environment for us all.

THE SUBSTITUTE (ALTERNATIVE) CHEMICALS PROGRAM: PURPOSE, ORGANIZATION, OPERATION

Leonard R. Axelrod, Ph. D*

In 1973, the House Appropriations Committee, Subcommittee on Agriculture-Environmental and Consumer Protection appropriated $5 million for fiscal year 1974 to the Environmental Protection Agency to "provide for research on and testing of substitute chemicals" (Public Law 93-135). The legislative intent for this Public Law and action can be found in the Congressional Record of November 6, 1973, i. e., "for the testing of substitute chemicals by EPA — to avoid taking action based on insufficient knowledge as has been done in the past."

Summation of this intent otherwise stated is to prevent the use of substitutes for deregistered pesticides which in essence are more deleterious than the original to man and the environment. The thrust of this legislative intent was derived from the uses of some 70 presently registered substitutes for DDT, but it also seeks to prevent such problems in the future when dealing with other substitutes now and in the future considered too hazardous for use in the United States.

The Substitute Chemicals Program has four principal objectives. The first is to identify suitable substitutes (alternatives), insofar as possible, for products and/or uses, both major and minor, which (a) are under internal review and therefore possible candidates for cancellation, (b) are in litigation for cancellation or suspension, or (c) have been canceled or suspended. The second involves studies to develop reliable and hopefully economically feasible screening methodologies for evaluating pesticides under review in the areas of

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*Director, Criteria and Evaluation Division, Office of Pesticide Programs, U.S. Environmental Protection Agency

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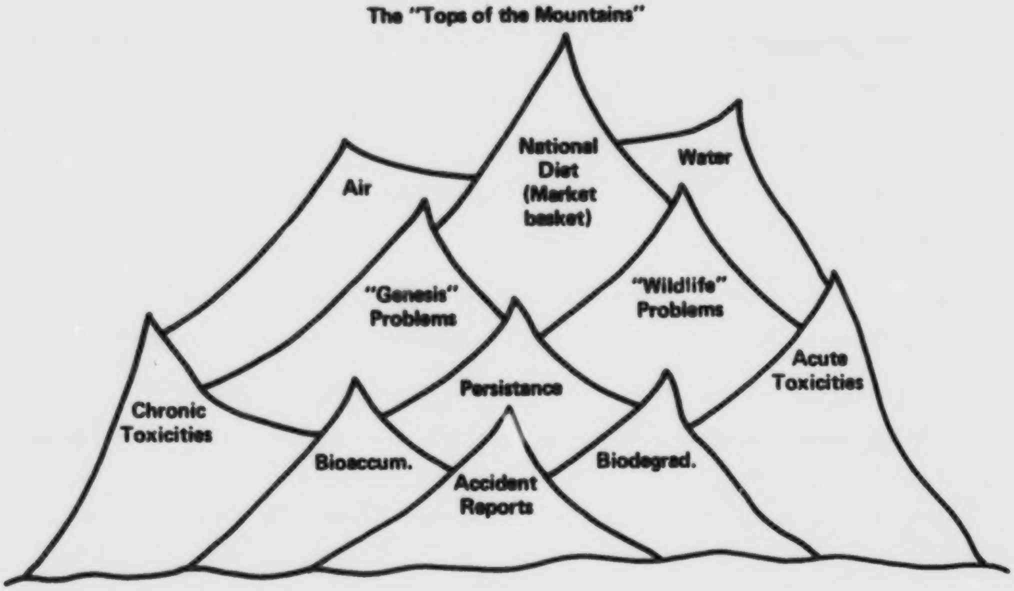
toxicology and safety, where there is such a need as for the "genesis" and reproductive problems. The third is to do research which fills certain gaps of knowledge in the areas of toxicology, ecology, and chemistry needed to flush out the data bases for the review of suitable substitutes. The fourth is to stimulate, through liaison efforts with industry, the research and development required to register new pesticides in specific areas of the agricultural sector needed as suitable substitutes.

Three subprograms have been developed:

The Reviews Process — First, the initial scientific review to study the relative safety of the substitute chemical. A look at the top of the mountains (Figure 1). Is there an obvious problem?

Figure 1

Initial Scientific Review

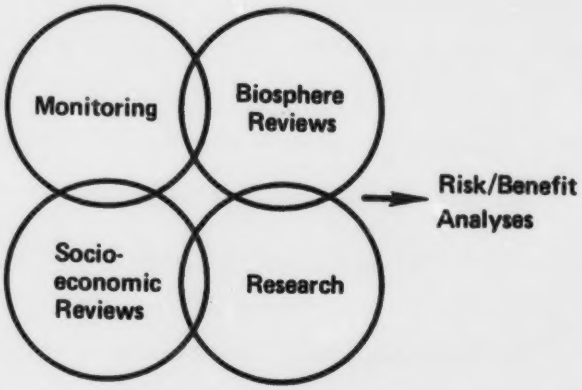

The "Tops of the Mountains"
National Diet (Market basket)
Water
Air
"Genesis" Problems
"Wildlife" Problems
Persistance
Acute Toxicities
Chronic Toxicities
Bioaccum.
Accident Reports
Biodegrad.

Second, the mini-economic review — an overview of the use patterns of a substitute and an estimate of the amount used annually in each pattern. This review identifies basic producers and performs an initial analyses of the economic benefits, by use, of the pesticide. It develops an initial view of the relative cost-efficiency data related to the pesticide uses.

If a problem seems to have emerged, then full biosphere and socio-economic studies are developed (Figure 2). If no problems are foreseen in the substitute uses and projected increased uses of the substitute, then the compound will be cleared through the reregistration process.

It should be stated at this time that a review of a substitute does not imply evidence of an adverse effect. It only means that the substitute has been apparently successful as an alternative to the canceled or suspended pesticide uses, or that it is likely to be put into place by the agricultural sector as an alternative.

Figure 2



Information Sources:
- Industry
- Academia
- Government
- International (e.g. WHO/FAO)

Actually, some confusion has existed with the term review in the Office of Pesticide Programs (OPP). There are four types of reviews progressing simultaneously in the OPP which are separate in thrust, intent, and meaning, as follows:

The registration review of a new pesticide seeks to review the data for both safety and efficacy as far as can be determined for a new pesticide use by present toxicological and environmental standards of testing.

The reregistration review, carried out in the Registration Division, seeks to determine if, after 5 years of use, the pesticide by company data and other exogenous inputs still passes the minimum required standards of safety and efficacy. It should be [illegible], however, that large numbers of pesticide registrations have never gone beyond an acute toxicity study and for those registrations on food and feed not beyond a subacute or 90-day study.

In the recent few years, certain chronic toxicity studies have been required and reviewed in registration for development of tolerances and ADI's for these pesticides, primarily for new pesticides. It should be pointed out that many presently registered pesticides were registered on the basis of required tests 10 to 25 years ago, and a different philosophy of the role of safety in man and his environment has since developed. The FIFRA, as amended, seeks to adopt new avenues of study for the reregistration process.

The internal review of a pesticide and its uses carried out in the Criteria and Evaluation Division initiates from extra-agency inputs such as major reports to the nation on health; Congressional inquiry either direct or through GAO; incidents leading to requests from environmental groups; NIH, FDA, and NCTR reports; or new data reported in the academic literature from laboratory or field experiences. Any or all of these types of reports have one thing in common. They report data for human incidence, animal experimentation, or environmental findings that imply unreasonable adverse effects to man or his environment. The internal review is developed to determine the credibility of these claims and the decision that if by all studies — economic, social, and scientific — the pesticide use still represents an unreasonable risk to man or his environment when compared to the benefits it represents, suggested action for cancellation or suspension of its uses be taken by the Administrator.

The substitute chemical program review carried out as a joint effort of the Criteria and Evaluation Division (C&E) and the Office of Research and Development (R&D) seeks to establish the credibility of a pesticide and its uses as a substitute for a canceled, suspended, or litigated pesticide and its uses.

The Liaison Effort is directed to all activities involved with research, development and manufacture, and use of pesticide products. Much of the liaison of the Alternative Chemicals Program will be conducted through this symposium and informal work sessions which will serve as the focal point for all information exchange and work priority setting. Liaison will be concerned primarily with the following:

- Present the progress of the various alternative chemicals research programs
- Identify data requirements to be derived from the various R&D sources available to the program to support the reviews
- Develop criteria for pesticide alternatives for special or unique uses
- Suggest solutions to special problems evolving from the review or scientific needs

The liaison program is envisioned to be beneficial in the following areas: (1) offer broad technical information and data support from government and industrial sources to the C&E staff performing the reviews for the program; (2) review, on an individual company basis at EPA, the results of the Initial Scientific and Mini-Economic studies; (3) expedite product and R&D efforts: and (4) aid in the retrieval of data not generally available in the literature or EPA files.

Finally, the third subplan, Research in support and development of substitute (alternative) pesticides. This program encompasses a considerable portion of the appropriation. Dr. Buckley and his group will present the main thrusts of the Office of Research and Development's areas of interest and concern. OPP has for the program needs, thusfar instituted studies on new, more effective, more credible and predictive screens for the genesis problem — primarily carcinogenesis and mutagenesis; studies on early warning systems for safeguarding and/or early alerting of applicators and users of hazardous levels of organophosphates and carbamates; and studies on a better understanding of the modes of action of the herbicides.

QUESTION: I understand this initial scientific review, the actual existence of four conditions of review.

DR. LEONARD AXELROD: I am glad you brought that up. Substitute chemical review as a part of initial scientific review. The other reviews, the registration, the reregistration, and the internal reviews have nothing to do with this aspect we will discuss today. There are other types of review in the Agency and we must not confuse these.

QUESTION: That's exactly the heart of the question. Are we talking about different people conducting the Substitute Chemical Program Review than those people that are conducting the registration reviews and so on and so forth?

DR. AXELROD: The registration reviews which are developed primarily on an ad hoc basis and are after October guided by guidelines for registration are done by one set of people, obviously in the registration division. The reviews which are internal, called internal reviews and substitute chemical reviews, are done by other scientists in the Criteria and Evaluation Division. But the thrust, the intent of these reviews is different, each to each own, and each to its own need, which I thought we brought out by talking of the credibility of claims made against a compound being in the "Internal Review" for the "suspect chemical" and saying that the alternative or "Substitute Chemical Review" deals only with establishing the credibility of safety of the compound with no claims made against this registered substitute.

QUESTION: I understand the philosophy of the whole thing but I have difficulty in assessing the idea that there are separate groups of people running these reviews which require a high level of expertise and knowledge about the individual products.

DR. AXELROD: I believe that we have people whose credentials would fit exactly the bill that you are discussing now. People who have pesticide and specific scientific expertise to carry out these, but they don't make decisions on their own necessarily. They do seek help from consulting areas, from industrial expertise, and from academic sources. It is not an individual's concept that goes forth from the Agency or from the Office of Pesticide Programs. It is a conglomerate decision.

DR. HENRY KORP: I can assure you these are different people. If my budget gets cut as it probably will, suspect chemicals may lose a few people, but I can assure you it will not be in the area of substitute chemicals. And that was a mission that was assigned to us by the Congress for at least 1 year and probably 2 years and that was kind of a fixed program to have a group of people to work on that without any question.

QUESTION: I wonder if this might not get to the heart of the problem and that is are the same facts and the same evidence to be used by these two different groups in connection with the same compound ?

DR. AXELROD: This same compound won't show up in the reviews. The compounds which are suspect chemicals have nothing to do with substitute chemicals. Those chemicals which are internally reviewed, given that name, are suspect chemicals. They are not on the program for substitute studies so the thrust, the intent, and the studies are quite different. Let's just take two I think we are all fairly familiar with called dieldrin and aldren. If we made a review of those compounds, they would be internal reviews. They would be compounds which were suspect due to one or more of these exogenous inputs of suspicion, but they would never show up as substitute compounds on this program.

Literally, the compounds we are looking at have not had any adverse mention from any source concerning their use pattern or their health effects. It is not the thrust of this program. So they are completely different compounds. You cannot have the same compounds showing up in both places.

QUESTION: In time sequence, however, you can indeed have them showing up in each place, I believe. First, the new compound is registered on the basis of all the required data and then as it's used over a period of time, it may become considered a substitute compound, and with further information it may very well become a suspect compound.

DR. AXELROD: That's correct.

QUESTION: Now, does it make sense then to have different groups of people review the same kind of information as this one compound progresses along this line of time?

DR. AXELROD: Because you have instituted an important factor, time, an expertise in a particular area, let's say a genesis area, may in 10 or 15 years be there to perform a different type of review. The possibilities of them being there are not that great but the kind of expertise he brings doesn't depend on himself, it depends on an information data base which is accrued in his professional life and information which has been accrued in the literature to support his ability to analyze that data base. The most important concept in science, whether it's in the EPA or not, is first to have data and then to have people who can scientifically review, analyze, and enunciate the decision based on that data, and it does not say, in any sense of the word, that there will not be argument and debate over any one subject. I don't know lawyers who think the same on all points and I don't know that scientists concur on the same points.

It was 25 years before Einstein's theory became hypothesis, and there were arguments as to the validity of his theory well into the 1930's although enunciated in 1905 by perfectly ethical expertise in the area of theoretical physics. So no one will stand and tell you that you will not have argument on two sides. It seems to me that in litigation proceedings that last 8 or 9 months, there are experts on both sides of the issue.

QUESTION: I don't even agree that there will necessarily be a time frame. You could be on both lists depending on what the suspicion is and could be suspect for one use and an alternate for another use.

DR. AXELROD: This is true but we are not viewing it and we are not willing to institute such a dualistic approach to the subject. We are trying to render unto Caesar what is Caesar's and a compound which is brought to our attention from the exogenous information sources as suspect will be treated as an internal review compound. It does not necessarily in any stretch of the imagination mean that it will be canceled. It only means that we look at it in the light of establishing the credibility, right or wrong, of the accusations. But it will not find itself on the list of substitutes, which doesn't exist officially.

QUESTION: But you hit on it and that is, did I hear you say that you could not or would not in the future establish a tolerance based on a 90-day chronic study?

DR. AXELROD: No, I didn't say that. I said that many of the presently registered pesticide compounds were established on no further studies than a 90-day study.

QUESTION: There is a distinct lack of that in section 3 of the present proposed regulations that it would imply that even negligible residue tolerances cannot be established. This has to be a complete change from what we were seeing, say 6 months ago.

DR. AXELROD: We are not really here prepared to discuss section 3. At this point in time, nothing of which we are presenting seems to have impact from the section 3 regulations. These studies are not regulated by section 3.

QUESTION: I wonder if you would comment on your point number four brought out on the stimulation of research and development. Does this refer to the stimulation of research and development as based upon your reviews on the alternate chemicals or new chemicals?

DR. AXELROD: The whole idea of research and development particularly in the industrial sector has emerged quite strongly over the last year to my knowledge, and it has been a subject of discussion not just with the Office of Pesticide Programs or ORD, but with the Administrator, to stimulate the industrial sector to bring to our agricultural uses new pesticides for these uses. And part of this program is to stimulate research and development to new directions exogenous to the Agency and that is, to fill data gaps where they exist and to literally anticipate as we go down the line, substitutes, alternatives for either compounds which don't seem to be effective as substitutes for deregistered products or canceled products, or in use areas such as minor-use areas where there doesn't seem to exist substitutes, i.e. effective pesticides for these minor uses.

QUESTION: Do you have any feel at all as to how many products you are going to be reviewing? Are you going to be reviewing one a year or 10 a year? Every product that's presently registered? After all, anybody can make an accusation against almost any product on the market.

DR. AXELROD: That's precisely the attitude which I think is negative and precisely the attitude we are trying to negatively delineate here. There is no accusation against the substitutes.

QUESTION: Do you have any guidance at all as to how big your program is going to be? Are you anticipating that you are reviewing one product a year or 10 products a year?

DR. AXELROD: We can only anticipate those number of products which can be reviewed according to the resource commitments made to the program, and that seems to stem directly from Congressional mandate.

QUESTION: Is that going to be one or 10?

DR. AXELROD: It won't be one and I don't know if it will be 10. It depends on how well things go. This is a new program. Much is to be considered for time. I certainly think it should be more than one just because you can do more with a few than you can do with one for the same manhour commitments.

QUESTION: My question goes back to what are the main objectives of the Substitute Chemicals Program. And as you define them, I understand they include defining substitutes for products that are under review, products that are under cancellation or some suspicion about them, and also products that have been canceled.

Now to me this puts all these products in the category that would be reviewed by an internal review concern, because an internal review is going on.

DR. AXELROD: "Internal Review" as I have enunciated is a review only for a compound for which negative information has been developed. Internal review only deals with a compound that could be classified as a potential baddy, not as a goody.

MR. DONALD McCOLLISTER: I think one of the things that's been bothering some of us is that if another DDT-type material is canceled and there is already registered a useful material that is commercially available and has a proper label for use on that crop, then the question is "Where does the Substitute Chemical Program come in?" As I read it, some of us have felt that the marketplace would just accept and use this other material.

DR. AXELROD: As it has.

MR. McCOLLISTER: But then all you've added, it seems to me, is this idea of establishing credibility. Now, I guess the only question is "How necessary is that step except that Congress told you to do it?"

DR. AXELROD: Well, you know, that's a good reason. I mean, we are a government agency. We are public servants and when someone says do it, you do it. He's going to give you all kinds of answers, but that's a good answer.

DR. KORP: Technically, it is a desirable thing to make sure that you are not using a substitute which may be even more hazardous than the material you have thrown out. That's really, as Len brought out, a secondary purpose. The fact is we've been given permission to do it, really, and not a mandate. It makes more sense to me.

DR. AXELROD: Let me say something which doesn't come into the purview of this delineated program but which is important from what you are saying. Judicious use of pesticides versus ludicrous use that was made of DDT and led to major problems existing, could be anticipated by this program. It isn't so much the compound you're using or how much is being used, as to what effects it has in our environment and in man. I suspect that if the word judicious use of DDT in all areas quantitatively and qualitatively had been implemented, we might not have gotten to the point where such accusations were made against the compound leading to its final cancellation, and I think it behooves both the industrial people and the government people to look at these substitutes now and for future uses to, hopefully, never have to bring forth such a massive accusation system and legal problem as existed with DDT. One pound used is one thing and 100 million pounds is another; whether it is persistent or nonpersistent is another, and various and sundry portions of the "tops of those mountains" bring to bear on whether this substitute may get into trouble as DDT itself did or whether that substitute is a suitable one.

One of our friends in industry has claimed over and over again that a substitute or alternative need not in any way be a real substitute for the stuff you are knocking out; that substitutes for canceled uses of 2,4,5-T may indeed not be as effective as the original compound and that fundamentally, at least in a theoretical consideration, there are no real substitutes for anything. However, there are registered substitutes.

DR. EDWIN ALDER: Dr. Korp, you have a mandate for a year or perhaps two from Congress for the Alternative Chemicals Program. If funds are available, do you see this as a program that would continue beyond the 2-year period?

DR. KORP: Of course, I have no way of knowing. It depends partially on our success. Will we really develop something in these first 2 years? Can we really develop information which will show these substitutes are better for the potential or will we have some products "knocked out of the box"?

We will certainly suggest continuing it if we find it's desirable. If it isn't, we'll say so. Budgets will be tight so I'd rather do those things that are desirable and necessary than just carry on a study because it's on the books.

QUESTION: The internal review is separate from the Substitute Chemical Program and you will not begin a review for a substitute until a product is "knocked out of the box," or if it's in the internal review you may pick it up at that point. What would you consider the reason the product ought to have a study made for substitutes?

DR. KORP: Because it is a widely made substitute.

DR. AXELROD: It's the mandate of the program. The mandate speaks that there is suspicion and it's backed up by law now and money for the law, that some of the substitutes or the substitutes for DDT were worse in the environment for man than DDT was, and with no accusations or fingerpointing there are many compounds — 70 in nature as I enunciated — which are registered substitutes for DDT.

QUESTION: My point is if you have a new compound, compound X...

DR. AXELROD: New compound means what in your way of thinking?

QUESTION: Well, a compound that's on the market and somebody says there's something wrong with this compound and therefore it goes into internal review.

DR. AXELROD: That's not a new compound.

QUESTION: It goes into internal review to see whether or not the accusations against it are valid.

DR. AXELROD: Yes, that's an internal review compound. That's not a substitute compound.

QUESTION: My question is now would the Substitute Chemicals Program then look at that compound and say, "It's under internal review, should we then begin to find a substitute, " or do you wait until there's a decision made in the internal review?

DR. AXELROD: I think it behooves the scientists in the Agency not to anticipate problems before they arise in this area. When a compound is in internal review and by risk-benefit analysis of rather in-depth studies for health, for toxicity, for man, for environment, and for socioeconomic consequences of taking it off shows that the risks are much greater than the benefits, I think it behooves us to start seeking out the presently registered substitutes, not necessarily to review them, but at least to enunciate those compounds which are presently registered as substitutes and hopefully to stimulate the industrial sector to seek compounds which may be better for the uses in question, and when one looks at internal review, it is not a matter of across-the-board either for enunciating the problems; it's a matter for uses. Use by use is looked at in the internal review for the hazards of the pesticide.

DR. JOHN BUCKLEY: It seems to me that maybe we have some misunderstandings of what seems to me a simple orderly process. You'll have ample opportunity to straighten me out on my misconception later on during the week, but the obligation of EPA in relation to pesticides was clearly stated by Henry Korp in his opening remarks. And that was that it's our job to see that there are adequate pest control methods of the optimum degree of safety available to the American public.

So you start the whole business at sort of a level of social trade-offs in terms of risks and benefits and there are a lot of things that go into that. One thing that goes into it is hard fact. That's presumably my part of the business — the generation of data, the validation of data, and its scientific evaluation. Resting on the facts there will be possible a whole set of decisions, some of which are never made. What's giving us trouble here is that we don't start at time zero with nothing having been done. It's an ongoing process. New compounds are being registered and the uses are being registered. Products are being reregistered. New facts are turning up and on demand EPA is looking at these to see whether the facts warrant some action or even if they are facts.

As a separate operation to increase the ability of the Agency to make sensible trade-off decisions as to what product will be available for which uses for a social gain of society, one of the things you want to know is whether, in fact, a proposed action is going to take you from the frying pan into the fire, and we clearly don't want to be there.

Now, I don't know that there's any instance in time, any exact event which would trigger a look at a compound as a substitute. It seems to me that if the evidence begins to mount that a particular product that has served us very well in terms of pest control is likely to have some severe problems and perhaps be less available, then at least an informal review starts. One of the things you have to know is what it will cost society. What will we have to get along without? What other things could be used? This program, as I perceive it, attempts to provide a factual basis for answering such questions. The program labeled Alternative Chemicals is an integral part of this whole business of providing the best possible social decisions.

Maybe "social decisions" is only another way of saying risk-benefit, cost-benefit, or whatever. You can't measure all factors in dollars. Some factors you really don't have good ways of measuring, but you can at least spell it out and include it as part of your consideration. That's what Mr. Korp gets paid for, making that decision or recommending that final decision.

My end of the Agency, my job, is trying to help provide him and his colleagues who reevaluate and write the criteria, with the best set of facts that will be helpful. The timing on this is regulated to some degree by the kinds of questions, some of which can be clearly enunciated today and some of which will arise after we leave this meeting.

DR. BARRY COMMONER: I would just like to add a few comments to what John Buckley said. When viewed against the background of the National Environmental Policy Act, the Substitute Chemicals Program takes on a rather general significance. Everyone is aware of section 102C of that Act which requires the preparation of an environmental impact statement for any major Federal program. A careful reading of that section and of the following one makes one realize that built into the Act is a firm requirement for looking at alternative ways of accomplishing a given program that might help minimize its impact on the environment.

It might help if we were to see how that approach works in an area that none of us here is directly connected with. Take for example, the environmental impact statement that the AEC filed on the breeder reactor. The statement has been criticized because it failed to look at alternative ways of producing energy — which is the purpose of the reactor. This kind of consideration really amounts to a new stage in the evolution of a national environmental philosophy; it points toward an approach that is positive rather than negative. After all, the fact is that you have to have electricity. Once that social necessity is recognized one can begin to see what range of alternative techniques are available for accomplishing that social goal, which minimize the resultant environmental hazards. The significance of introducing alternatives into these considerations is that it sets the social goal as the target (in this case producing energy) and looks for the best way of achieving it.

The SCP represents the extension of this new, positive approach to the pesticide field. Although the SCP arose out of a response to the environmental challenge to DDT, I believe that it will have a much wider significance. What the SCP can do is to give society a wider range of alternative ways of accomplishing what a pesticide is supposed to do — which is to improve food production, for example. We ought to look at the program as a positive one, rather than as an extension of the adversary approach that has been charactersitic up to now. What the SCP does is to extend the scientific base that will be available to us as we seek to accomplish the social purpose toward which pesticides are, in principle, directed — the improvement of human welfare.

THE ALTERNATIVE CHEMICALS PROGRAM: FLOW CHARTS AND KEY DECISION POINTS

Mr. Kenneth O. Olsen*

The work-flow chart and key decision points that will be discussed this morning reflect the safety reviews of registered substitute chemicals that will be performed under the Alternative Chemicals Program. These safety reviews are a major thrust of this program, and the decisions made during the review determine the suitability and acceptability of a particular registered pesticide to act as a substitute chemical.

There are several other major decisions that must be made independent of the safety review of an individual registered substitute chemical. The development of testing methodologies and techniques, other related research programs, and liaison activities with industry, academia, and other government agencies are examples of these. Details of these projects will be provided later in the program. These other activities and projects within the Alternative Chemicals Program have been carefully evaluated, along with requirements of the safety reviews, in order to obtain maximum program benefits within the appropriated resources.

It is very difficult to establish a detailed safety review procedure which can be applied across the board to every registered substitute chemical. The type of pesticide, its use patterns, and the availability of scientific and economic data are just some factors which influence the scope and resource commitment of an individual review.

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*Program Manager, Criteria and Evaluation Division, Office of Pesticide Programs, U.S. Environmental Protection Agency

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What will be presented next is a general work-flow procedure which is representative of the safety review of most registered substitute chemicals. This procedure has been broken down into two phases in order to consider all possible decision-making options that might arise during the review process.

Phase one of the review evaluates the safety of the substitute chemical based on existing data bases. Phase two performs a detailed risk-benefit analysis of present and projected uses of the substitute chemical (Figures 1 and 2).

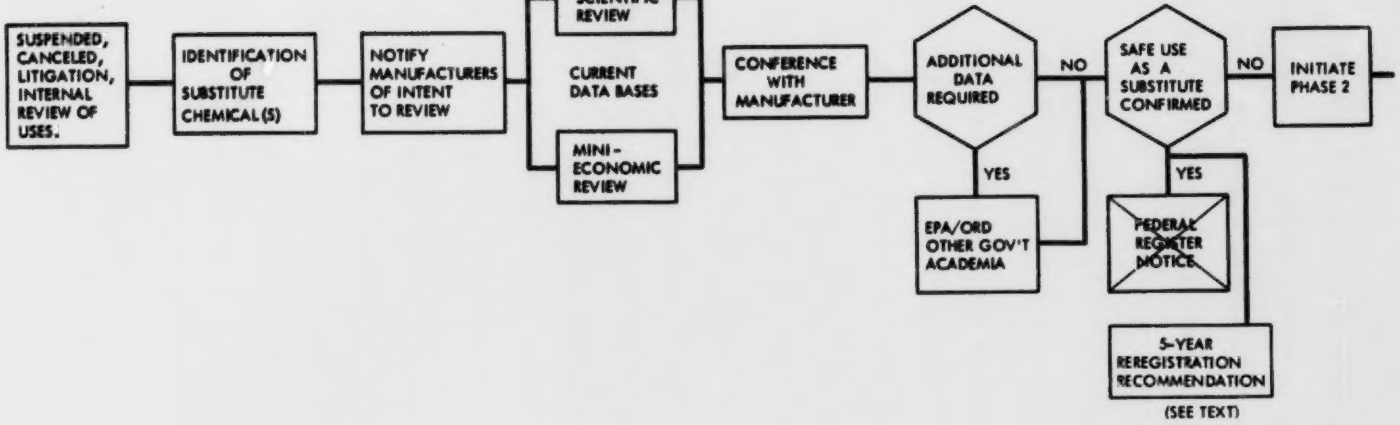
Block 1 indicates the identification of those pesticides and their associated problematic uses that require substitutes. These pesticides are identified from pesticides that have been suspended, canceled, or in litigation, or during the latter stages of the internal review being conducted in the C&E Division.

The second block identifies registered substitute chemicals for those potentially problematic chemicals identified in block 1. At this point in the work flow, those uses of a problem pesticide that have been canceled, suspended, or in internal review are listed. The EPA "Compendium of Registered Pesticides" is then searched to determine which registered pesticides have one or more concurrent substitute uses. A matrix of uses is prepared and all of the registered substitutes that have been registered for those particular uses are listed. In some cases we may have a substitute chemical for several uses of a canceled product and in other cases we may have a substitute for just one use.

These substitute chemicals are listed in order of priority for the review process, and we begin the review processes on the first priority substitute pesticide. Before starting a safety review of a registered substitute chemical, we will notify by letter the manufacturer or manufacturers of that chemical of our intent to review it. The letter will state as a minimum, an overview of the Alternative Chemicals Program, the uses that are registered as a substitute, and the approximate time frame for this phase one of the review. These letters will be going out very soon. I would expect by the end of next month.

Figure 1

ALTERNATIVE CHEMICALS PROGRAM
Substitute Chemical Review - Phase 1


SUSPENDED, CANCELED, LITIGATION, INTERNAL REVIEW OF USES.
IDENTIFICATION OF SUBSTITUTE CHEMICAL(S)
NOTIFY MANUFACTURERS OF INTENT TO REVIEW
INITIAL SCIENTIFIC REVIEW
CURRENT DATA BASES
MINI-ECONOMIC REVIEW
CONFERENCE WITH MANUFACTURER
ADDITIONAL DATA REQUIRED
YES
EPA/ORD OTHER GOV'T ACADEMIA
NO
SAFE USE AS A SUBSTITUTE CONFIRMED
YES
~~FEDERAL REGISTER NOTICE~~
5-YEAR REREGISTRATION RECOMMENDATION
(SEE TEXT)
NO
INITIATE PHASE 2

Next the C&E Division review team will perform the initial scientific review and mini-economic review of the substitute chemical. Dr. Axelrod has touched on these reviews and they will be gone into in quite a bit of detail in the afternoon session by Dr. Burkhalter and Mr. Conopask. They essentially look at factors such as the chemistry, toxicology, pharmacology, fate and significance in the environment, broad use patterns of the pesticide, and the economic benefits of the pesticide to the user.

Upon completion of these two reviews, copies will be sent to the manufacturers of the substitute chemical for their review and comment. The manufacturer will not be under any obligation and will be asked to respond strictly on a voluntary basis. Each manufacturer will have the option to evaluate the data requirements and to supply additional data he might have available which would assist us in the review process.

If the manufacturer desires, a meeting will be held at EPA to discuss the safety review. This meeting will be scientific in nature. C&E will have the members of the review team available to discuss the scientific aspects of the review. No EPA policy or potential decisions on the suitability of the substitute will be discussed at this meeting.

This brings us to the first key decision point in the program. At this point in the review process we will have retrieved information from all known existing data bases and from the manufacturer. Key C&E scientific personnel will then evaluate the review to determine if this data base is complete enough to make a decision with respect to the suitability of the registered substitute chemical. If it is determined that additional data is required, several sources will be contacted. If the data base is judged to be complete, the safety review will continue to the next key decision point.

The missing data for a review can now be clearly defined. If the missing data is not obtainable from the manufacturer in a reasonable time frame, several other sources will be utilized to fill these data gaps. Dependent upon the nature of the missing data, EPA's Office of Research and Development (ORD) will be contacted. ORD will play the major role in the effort to obtain missing data. Academia through grants and contracts may also be contacted, as well as private contractors.

Now if there is a time delay in obtaining the missing data — that is, if it's dependent upon a test method development or some long-range testing that has to be done — the review team will go back to the use matrix derived in block 2 and begin the initial review of the next pesticide in order of priority. I would like to mention that there are several other research efforts already initiated by ORD within the program that can be applied to the evaluation of all substitute chemicals.

Once the data has been obtained (if it's needed), we go to the next decision point, which is safe use as a substitute confirmed. This is the second key decision point in the work-flow chart for the review process. The issue here is, essentially, in the viewpoint of key scientific personnel within C&E and ORD, have the initial scientific and mini-economic reviews proven the suitability of the chemical to be an acceptable substitute. If yes, EPA will place a statement to this effect in the Federal Register. It will say compound X has been evaluated by EPA and found to be an acceptable substitute for the canceled or suspended uses of the original compound. *

If the answer to the safe use as a substitute cannot be confirmed, we proceed one more time to the right on the flow chart and do not make any public statements as to the relative safety of the substitute chemical. A

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*Note: Since the Denver Symposium, OPP has reevaluated the issuance of this notice and decided to delete it from the program. In its place C&E will recommend to the Registration Division of OPP that a 5-year reregistration be granted the pesticide under review and the manufacturer be notified once it is approved.

detailed risk-benefit analysis will be performed next on the present and projected uses of this particular substitute. This in effect initiates phase two of the review process.

Perhaps before I go into phase two, if anybody has any quick questions on phase one, I will be glad to answer them.

QUESTION: What impact or what relationship will this have to a cancellation proceeding or a suspension proceeding which might be ongoing? Because the first box indicates that that would be going on. And what role would that play in the cancellation proceeding or any other proceeding?

MR. KENNETH OLSEN: Well, it would have impact in that if we found a relatively safe substitute for the pesticide, that would be brought up during the hearing. And, negatively, if we couldn't find any suitable substitutes, that might have an impact on the future decision of the Agency.

QUESTION: But would the hearing go on independent to this program?

MR. OLSEN: Yes. It's completely independent. It's carried out by the Office of General Counsel of EPA.

QUESTION: What would happen in the event that the hearing determined on its own, as has been done in the past, that there were substitutes available, and their decision was to cancel the product, and your decision was contrary to that or the reverse?

MR. OLSEN: Well, we would maintain coordination with the hearing at all times, and we would try to avoid this type of decision. During a litigation, if certain substitutes were identified, we would attempt to answer the question as to whether those substitutes are safer or more hazardous than the compound that's in the hearing.

MR. MEL GARBETT: What's the criteria for the order of priorities in the selection of the substitutes?

DR. AXELROD: The amount that one uses of the substitute, the number of uses for the substitute and the specificity of or the exclusive use of a substitute, and the economics of those uses would set up the matrix of the priority.

MR. ROBERT HAMMAN: I have a question concerning the Register notice. Your review a compound which is registered on corn, for instance, and decide that it is a good substitute. You publish this in the Federal Register. What happens if you decide "no"? Does the Registration Division have to consider cancellation of that product's use?

MR. OLSEN: No, that initiates the phase two of the review. No Register notice will be placed if we say no. I'll get into that during the second phase of the review.

We'll start here with the answer being no Federal Register being placed (block 1). This initiates the comprehensive biosphere review of the compound. We also perform a socioeconomic review which assesses the net benefits and costs of the chemical at present and in the future. These reviews will be discussed later in today's afternoon session by Drs. Dale and Aspelin.

At the completion of the biosphere and socioeconomic review, we come to the third decision point, which is safe use as a substitute confirmed. This is essentially the same block we had in the phase one review. Now we have considerably more analysis and data to make that decision.

If the suitability of the substitute chemical can be confirmed at this point, a Federal Register* notice will be published as before. If not, we

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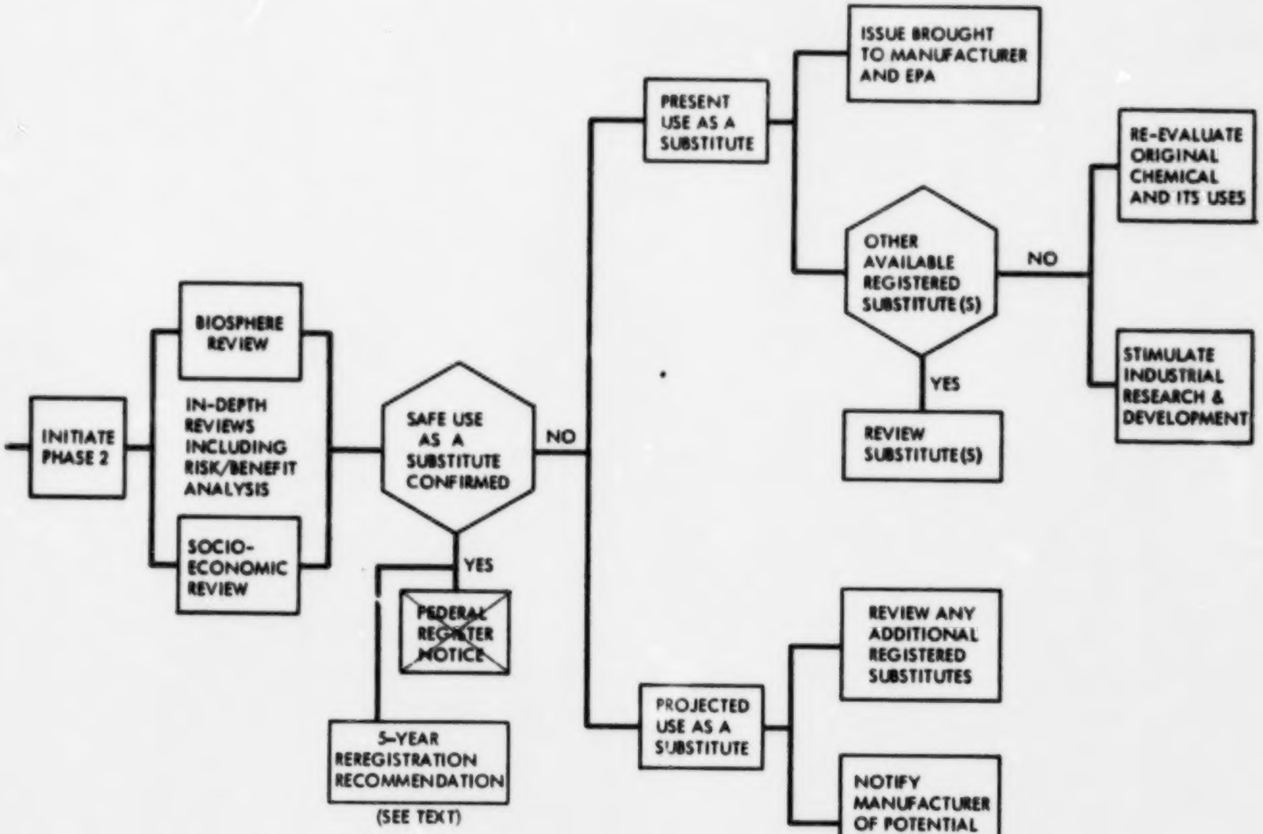
*Note: Since the Denver Symposium, OPP has reevaluated the issuance of this notice and decided to delete if from the program. In its place C&E will recommend to the Registration Division of OPP that a 5-year reregistration be granted the pesticide under review and the manufacturer be notified once it is approved.

Figure 2

ALTERNATIVE CHEMICALS PROGRAM
Substitute Chemical Review - Phase 2


INITIATE PHASE 2
BIOSPHERE REVIEW
IN-DEPTH REVIEWS INCLUDING RISK/BENEFIT ANALYSIS
SOCIO-ECONOMIC REVIEW
SAFE USE AS A SUBSTITUTE CONFIRMED
YES
~~FEDERAL REGISTER NOTICE~~
5-YEAR REREGISTRATION RECOMMENDATION
(SEE TEXT)
NO
PRESENT USE AS A SUBSTITUTE
ISSUE BROUGHT TO MANUFACTURER AND EPA
OTHER AVAILABLE REGISTERED SUBSTITUTE(S)
NO
RE-EVALUATE ORIGINAL CHEMICAL AND ITS USES
STIMULATE INDUSTRIAL RESEARCH & DEVELOPMENT
YES
REVIEW SUBSTITUTE(S)
PROJECTED USE AS A SUBSTITUTE
REVIEW ANY ADDITIONAL REGISTERED SUBSTITUTES
NOTIFY MANUFACTURER OF POTENTIAL PROBLEM IN FUTURE

have to evaluate the results of the risk-benefit analysis that was performed. This analysis is essentially forward looking with respect to the present and projected future uses of the registered substitute chemical.

If the present use or uses of a registered substitute chemical present certain problems with respect to safety, two parallel actions are initiated. (See upper right area of Figure 2.)

The first of these is the identification of a problem with the present use of the substitute. This problem is defined and communicated to the manufacturer and other areas of EPA. OPP prepares a report based on scientific data which outlines the potential problem strictly on a scientific basis. Simultaneously, the use matrix that was prepared during phase one is consulted and OPP initiates the review of an additional substitute, if one is available.

If no other substitutes have been registered, two additional actions are initiated. The first of these is a reevaluation of the original decision to cancel, suspend, or impact the internal review of the original compound. The second of these is to stimulate, through liaison efforts, the industrial research by providing some sort of a need statement for a substitute chemical, with respect to a particular use of a deregistered or suspended product.

If the risk-benefit analysis says essentially the present use of the substitute is suitable, but indicates out in the future you might have a problem, two additional parallel actions are initiated. (See lower right of Figure 2.) The first of these is to go back to the use matrix developed during phase one, go to the next substitute in order of priority, and begin the review process for this next substitute. In addition, only the manufacturer of the substitute chemical that has just been reviewed will be notified of the identified potential problem with his particular pesticide when used in the substitute role. This will provide the manufacturer with some lead time to correct this potential problem before it occurs.

That about concludes the phase two of the review. I have tried to keep a few minutes for questions and answers. I've run through this maybe a little fast in order to maintain schedule, but do we have any questions on phase two or on the entire review process?

QUESTION: It's already been discussed and mentioned several times that there were 70 substitutes for DDT. Now DDT has been canceled. It seems to me that if this scheme is going to be used, the first matter before the house is to review those 70.

DR. AXELROD: It's substitutes for a particular use that we're discussing. It narrows down the field very, very considerably when you set up these reviews. So, it isn't a matter that 70 compounds have been enunciated for all uses simultaneously to DDT. It's a matter that DDT was so ubiquitously useful that into the marketplace came those already established or new ones, which for some uses would be DDT substitutes. What we address there are those uses, not a coverall for all uses.

QUESTION: Yes, but I think that the action against DDT was pretty much for all uses.

MR. OLSEN: That's right, but the substitute chemical reviews are on a use-by-use basis. They're not across-the-board reviews of all uses of DDT and those substitutes that have been identified.

QUESTION: I'm not quite sure whether this is a question or a statement. But if you will publish all of the substitutes that are available, as you said, is this not just a restatement of the registration process, which states that these uses have been examined and found capable of being registered.

DR. KORP: I agree with you. But, as pointed out, once you have given this a special blessing because it's gone through a review process, everybody doesn't know about all those that are registered that might be desirable. I don't know what will happen yet. It might be desirable to show that there are these compounds plus others available for this particular use.

OFFICE OF PESTICIDE PROGRAMS LIAISON

Frederick W. Whittemore, Ph.D. *

In the few minutes which I have this morning, I would like to talk to you for just a short time about the functions and responsibilities of the Operations Division and how they relate to the Alternative Chemicals Program. The Operations Division is responsible for the development of programs designed to enhance the effectiveness of government activities in the pesticide area. In carrying out these responsibilities, it provides program policy direction to the technical assistance and training programs and to the gathering of information on the consequences of pesticides use. And it is in this particular area that we have a direct relationship to the Alternative Chemicals Program.

Of particular import in these responsibilities is the outreach aspect, which provides EPA with liaison outside of its headquarters structure at two levels, national and state. In dealing with the various responsibilities of the Operations Division, we have chosen to organize it into two branches. One, a liaison and training branch, and the other a pesticides use consequences branch.

It is important to recognize that although EPA is responsible for the administration of FIFRA, the Agency is only one facet of a rather complicated national system of pesticide use and management. The Agency has the dual and sometimes conflicting role of assuring maximum safety and environmental integrity while being responsible for maintaining workable processes of registration, regulation, and enforcement which provide the public with needed chemicals and associated devices.

The ten regional offices provide a national network which facilitates the process at the state level. First, at the national level, the Operations Division is responsible for maintaining coordination with a number of Federal agencies,

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*Acting Director, Operations Division, Office of Pesticide Programs, U.S. Environmental Protection Agency

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most particularly with the U. S. Department of Agriculture. In accomplishing this coordination effort, we actively participate and support the Secretariat of the Federal Working Group on Pest Managment and have EPA representation on the appropriate panels of that working group. (Panels have to do with such subjects as monitoring, research, categorization, training, things of this type.) We also have within our division, a Federal Agency Liaison Officer who has direct responsibility to maintain liaison with these other Federal agencies.

On an ad hoc day-to-day basis we, of course, have very close liaison with Agriculture, the Agriculture Research Service of Agriculture, the Extension Service, and the Forest Service.

A typical example of our liaison activities with, for example, the Extension Service, is a recent decision by the Administrator of EPA, Mr. Train, and the Secretary of Agriculture, Mr. Butz, to seek supplementary funding for the training and certification of pesticide applicators required for the implementation of FIFRA by the rather magic date of October of 1976, by which time state programs for the certification of applicators must be in place and applicators must be certified if they are to use restricted-use pesticides.

With respect to headquarters liaison with national organizations and programs, we again have a number of national organizations in which we actively participate and have representation. The first of these is the National Association of State Departments of Agriculture. In the last 6 weeks, Dr. Osmun has attended four regional meetings of this organization to explain the implications of section 4 and the legal authorities that states must have to license and certify applicators.

We have also had meetings with the American Association of Pesticide Control Officials. These are representatives of the state agencies responsible for the regulation of pesticides within the states. In addition, we have had a number of interchanges with respect to OPP and EPA responsibilities in the area of pest management strategies, and the Office has sponsored one project in California on the integrated pest management of production tomatoes. There are also other national organizations with which we have very strong and close contacts, such as the National Aerial Applicators Association and the National Pest Control Association.

With respect to liaison at the state levels via the regions, EPA has ten regions throughout the country and our contacts with the states are via those regions. In each one of the regions we have a Pesticides Branch Chief. Certainly with the implementation of FIFRA and especially with the implementation of section 4 and the program for state certification of applicators, it will be essential to involve the regions in this program.

I mentioned earlier that we have within the division a liaison and training branch, and the activities which I have been discussing up to now have been specifically related to that branch. In addition, we have a pesticides use consequences branch, and within that branch we operate what is known as PASS, the Pesticide Accident Surveillance System.

This activity, of course, involves recording accidents as they occur and assembling data on accidents with the view of establishing or identifying major problems and, hopefully, coming up with suggested solutions to those problems as they may relate to packaging, formulation, and registration.

Of even greater importance, however, are other activities of this branch which, quite frankly, have not yet been fully defined. These have to do with the subtle, currently unrecognized events that may be taking place as a consequence of pesticide use. If we knew all of the devils that there were in all of the pesticides with which we are dealing, our problem would be simple. But the fact remains that some of the compounds about which we know the most — and, I'm referring here specifically to DDT — have virtually passed from the scene.

We have a long use experience with DDT and some of these other older compounds. Our use experience with some of the more recent compounds is very limited, and possibly there are many hidden devils in these newer compounds which are completely unrecognized at this particular point in time. This to me is a very important aspect of the results of the consequences and the changing patterns of pesticide use.

It is in this area, I think, that we have a very close relationship with the Substitute Chemicals Program, because certainly some of the chemicals which can be considered as substitutes do not have the long history of use either in this country or abroad by which such problems can be identified. We may have many unrecognized problems with some of these so-called substitute chemicals.

In summary, the Operations Division has two main functions: First, liaison and training, with particular reference at the moment to the training and certification of pesticide applicators to comply with the provisions of the new FIFRA. Secondly, pesticide use consequences, with current emphasis on what we call the Pesticide Accident Surveillance System. I would hope longer-term emphasis would be upon the consequences of pesticide use and some of the unrecognized hazards which undoubtedly still exist in some of the new compounds.

QUESTION: Perhaps I misunderstood some of the things that you were saying, but it seems to me that one of the thrusts of what you said was that in the exploration of the substitutes, it would be important to look for hidden problems that may exist with some of the substitutes, if not all. Is this not contrary to the program as Dr. Axelrod described it? I struggle everyday to look for a positive attitude. This one's a little confusing.

DR. FREDERICK WHITTEMORE: Well, if we could identify the devils, they wouldn't be unknown. But I am firmly convinced, having had some experience in this, possibly for 35 years, that the devils that we know are better than the devils we don't know. Because, if we know the devils, we can identify them and we can cope with them. After all, I have been in this work ever since 1941 and was probably one of the first ones to use DDT on a broad scale in North Africa and in Naples in 1943.

And I keep going back to the proposition that if we know the devils, we can recognize them and we can contend with them. It's the devils we don't know that are hidden in these compounds that we really should start worrying about.

I can recall it wasn't too long ago when people didn't worry about residues of parathion. We thought that parathion residues more or less disappeared. It wasn't until maybe 4 or 5 years ago that we recognized that maybe residues of parathion on food commodities would be a problem for as long as 30 to 45 days after application. And I repeat again, if we know the devils and we can recognize their magnitude, we can deal with them. It's the unknown devils that we should worry about in certain instances.

MR. ALFRED MITLEHNER: In line with what you're saying, is it reasonable to suggest that the modification of a use pattern of a suspect chemical might indeed be the best alternative to that particular situation and that this should be a part of the Alternative Chemicals Program, in addition to looking for different chemicals?

DR. AXELROD: I guess we can speak from present experience in the C&E Division, where internal reviews of suspect chemicals are being conducted, that indeed we're not looking across the board. Hopefully, not to make the kind of errors we have in the past been accused of with DDT, but looking separately at the various uses. And I think that we're getting a better appreciation for that separate look at certain uses, which might mean further work on the part of the

Agency but not across the board. That modification of use patterns might indeed be one way to go to remove the substitute or suspect chemical from that suspicion. But I'd like to give much more thought to that.

DR. JERRY SMITH: Would not a rational, non-abrupt alteration in the use pattern of a pesticide suspect of being hazardous, bring in competition? Would not free enterprise provide the alternate or substitute chemical? That is, as we gradually withdraw a pesticide from use, will not new registrations themselves take care of the problem?

DR. KORP: The problem you face is that you tell us 7 years and $10 million. In other words, I don't want to have a 7-year hiatus. In other words, at least we ought to be looking. I mean, I don't disagree with you; I'm just saying that it isn't something that you can snap your fingers and have something fill in. So if we look, we're just simply trying to accelerate the process.

DR. SMITH: What we're trying to do is to prevent the abrupt removal of a pesticide from the market, leaving a void. If something has been on the market for years and years, you don't all of a sudden...

DR. KORP: No, I won't accept that statement. That's not a fair statement — the fact that something got on the market, in other words, erroneously. You'll have to remember that we have new knowledge, new opinions, and new everything. In other words, we've got to look at these things based on the current situation, not what it was back in 1908.

DR. R. E. HANSON: I think the question's directed toward Ken, but there is a point in there where there's a meeting with a manufacturer. Now let's take a proprietary compound, and for whatever reason we disagree with your assessment of a substitute and we say no way will we have anything to do with registration of that product as a substitute. What happens to the Substitute Chemicals Program then?

MR. OLSEN: The meeting will be held on already registered substitutes. We're evaluating a registered substitute, not a new compound.

DR. HANSON: No, I'm talking about an old compound, but not registered for that use.

MR. OLSEN: Well, it will be registered for the use and that would be a viable substitute.

DR. HANSON: So, you will not be looking at a non-registered compound.

MR. OLSEN: That's right.

DR. HANSON: Somewhere in that chain of events though, when I unravel what all those charts mean, there must be that too.

MR. OLSEN: Right. Well, that's toward the end of the review where we identify that no substitute is available.

DR. HANSON: No registered substitutes.

MR. OLSEN: No registered substitutes. First, we look at all the registered substitutes by use.

INITIAL SCIENTIFIC REVIEW

Thomas D. Burkhalter, Ph. D. *

The initial scientific reviews present general discussions on potential human and environmental safety considerations of registered alternatives for uses of a pesticide that have been suspended, canceled, or are described as being suspect.

The scientifically oriented review relates to broad methods of pesticide applications and includes all uses of the product (Figure 1). The objectives of the review are mainly two-fold, whether conducted on alternatives for canceled use or on alternatives for a suspect use product (Figure 2). These objectives are to analyze the safety factors for the substitutes as a basis for a decision to proceed with a more comprehensive biosphere review and, secondly, to describe areas in which technical data are lacking so that appropriate studies can be initiated to develop definitive information.

Figure 1

Initial Scientific Reviews

Purpose:

1. Review safety aspects of registered substitutes for canceled pesticide uses.
2. Review safety aspects of registered substitutes for suspect pesticides.

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*Head, Plant Physiology Section, Plant Studies Branch, Criteria and Evaluation Division, U.S. Environmental Protection Agency

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Figure 2

Initial Scientific Reviews

Objectives:

1. Determine need for further reviews.
2. Define knowledge gaps.

The initial scientific reviews are conducted by multidisciplinary teams comprised of scientists in the field of chemistry, toxicology, wildlife biology, ecology, and disciplines to which the pesticide uses belong, such as entomology, plant pathology, and physiology (Figure 3).

Figure 3

Initial Scientific Reviews

Scope:

1. Multidisciplinary teams
2. Chemistry, use methods, and toxicity

Presently, insecticide and herbicide teams are preparing to review registered alternatives for the canceled uses of DDT and 2,4,5-T. If the initial scientific review is for an alternative pesticide use substituting for a canceled use, the factors may be considered to center on those relating to the reasons for cancellation: This could be persistence, toxicology, or bioaccumulation. If the review is for uses of alternative pesticides for a suspect product, the subtitute's safety is to be verified.

The data to be reviewed relate predominantly to chemistry, use, and toxicity, which are interpreted according to the character and method of the use of the product.

The initial review for chemistry involves four major categories involving physiochemical properties, analytical methodology, residues for food and feed, and, of course, the environmental aspects (Figure 4). Physiochemical properties include those areas in which, for example, synthesis and production technology are considered in terms of intermediates, wastes, and side reactions which may pose adverse effects.

Figure 4

Initial Scientific Reviews

Chemistry:

1. Physiochemical properties
2. Analytical methodology
3. Residues in food and feed
4. Environmental

Secondly, the composition of the technical and the formulation is considered. Physical properties, such as melting point, boiling point, specific gravity, vapor pressure, and partical size are under consideration as well as chemical properties and reaction, such as degradation reactions and chemistry of metabolities, decomposition reactions and processes, hydrolysis, thermal decomposition, photalysis reactions, pH and stability, and oxidation reactions.

The analytical methodology is concerned with acceptable methods involving reproducibility and sensitivity, and for regulatory purposes satisfies enforcement needs. Methods are evaluated not only for the active chemical, but also for the principle degradation products, as delineated in the above processes. These are to include analytical procedures for food and feed crops, water, soil, and biological entities.

The method should have specificity to pick out the chemical or degradation product from mixtures. Analysis of pesticides in corn, for example, may yield several pesticide chemical entities used on the crop. Each chemical should be distinguishable from the other.

In terms of residues in food and feed, considerations on residues involve several distinct areas: the occurrence of pesticides in food and feed crops; the relationship of residues in food tolerances established and food tolerances pending; the relationship to acceptable daily intake; and the results of monitoring programs, including FDA market basket study and the USDA consumer and marketing studies.

Environmental considerations are, of course, always paramount. The fate, movement, and transport of pesticides in the environment is a focus of many concerns. This involves a potential for secondary effects particularly on the non-target areas resulting from the chemical or its important and toxic metabolites. These areas include persistence and toxicity of the chemical and its metabolites, leaching of the chemical or the toxic metabolites out of the target area, bioconcentration in a species, and bioaccumulation of the chemical or its metabolites through the food chain.

The toxicity evaluation of a pesticide cannot be underestimated and is intended to include toxicology, pharmacodynamics, species behavior, records, and potentials (Figure 5). For toxicology and pharmacodynamics, the first information one thinks of is the toxicology of acute, subacute, and chronic effects. These normally involve toxicity to laboratory animals and to domestic animals. Toxicology efforts are not limited to these and continue in symptomology, pathology associated with animals, toxicity to fish, toxicity to other aquatic species, toxicity to wildlife, and metabolism including absorption, distribution, excretion, and biotransformation.

Figure 5

Initial Scientific Reviews

Toxicity:

1. Toxicology and pharmacology
2. Species behavior
3. Records and potentials

Also, the genic effects are carcinogenic effects, tratogenic, mutagenic, and tumorogenic effects. Species behavior is considered in effects on reproduction in laboratory animals, domestic avian species, and crustaceans, and, of course, in behavioral effects.

Records and potentials include such things as field exposure evaluations, ecological imbalance effects, and incident records.

Use aspects are always important and they include, generally, application rates, patterns of use, methods and applications of timing, drift, exposure, and form in which it is applied as in EC or dust or granule (Figure 6). The development of use aspects of a pesticide involves first a collection of the registration history. This includes Federal Registration, state cancellation and suspension actions, and the highly informative state recommendations, which reflect commonly recognized practices.

Figure 6

Initial Scientific Reviews

Use Aspects:

1. Application rates and use patterns
2. Application methods and timing
3. Formulation in which applied

The collected information provides a record of label and labeling for each use, which acts as a basic source for all use aspects and generally includes these points: currently registered uses both on cropland and on non-cropland, including previously registered uses which have been dropped by the sponsor, canceled, or suspended; dosage rates currently accepted by the registration division (this may also reflect those instances in which recommended dosages of an established product have been increased or decreased at the request either of the sponsor or of the Agency); formulation including the form in which a product is available for each use and dosage, such as wettable powders, granules, dusts, emulsifiable concentrates, flowable suspensions, and so forth; the frequency of application, the number and time between applications; timing of the application, including dormant, prepliant, preemergence, and so forth; specific application directions and techniques such as soil incorporation, subsurface metering into irrigation water, or air application.

Of critical importance are the label directions and limitations designed to further assure safe, effective use. These include preharvest intervals, rotational cautions, geographic restrictions, and land use limitations.

Other information is also collected which impinges on the use but is not necessarily reflected in the labeling. State, regional, and more local actions to restrict or deny use of a particular pesticide are considered. Actions at the state and local levels to promote and recommend, particularly for uses not Federally registered, are also considered.

Information on all these aspects surrounding the use of the pesticide is obtained from a variety of sources. Some of the most important are Technical Services Division data base and bibliographies, EPA registration files, Federal and state research stations, pesticide manufacturers, trade associations, and scientific literature.

On completion and evaluation of the initial scientific review, each registered use of an alternative for a suspect or canceled pesticide is examined in terms of the data assembled (Figure 7). The team leaders may elect to use consultants. One of the following courses of action is then taken for each alternative pesticide, as described this morning by Mr. Olsen.

Figure 7

Initial Scientific Reviews

Actions:

1. Safety confirmed
2. Insufficient data for decision
3. Safety questionable

When the safety is confirmed, this decision concludes that an alternative pesticide use reviewed for safety may be considered an acceptable substitute for the canceled or suspect pesticide use. The decision, therefore, verifies that the alternative is acceptable as intended.

There is, of course, an interim decision when there is insufficient data to decide. Significant data gaps are defined and appropriate investigations initiated to determine if the information in the normal registration process or unpublished data exists to fulfill these gaps. If not, research needs will be delineated, as well as input from other sources, as indicated this morning by Mr. Olsen.

The third decision is the decision of questionable safety. This decision initiates a comprehensive biosphere and socioeconomic review of the substitute pesticide use. This aspect of the review will be described later on this afternoon.

THE MINI-ECONOMIC REVIEW

Jeff Conopask*

In assessing the substitutability of a chemical for those registered pesticides for which adverse legal action has been taken by the Agency, it is most important to analyze the basic economics at the user level. Such questions as the following will be asked: Are there economic substitutes? Will the chemical production industry be able to produce substitutes in adequate quantities as demand increases for these chemicals?

The purpose of the mini-economic review is to provide an initial assessment of these questions. The approach is to consider both the supply and demand sides. A more detailed analysis may be required later, if significant environmental problems are found to exist from the initial scientific review.

On the supply side, the basic concern will be whether or not the industrial capacity of producing a substitute chemical is commensurate with a potential demand for that chemical. Figure 1 shows that we need a number of data points to analyze this aspect. They include the following: total production level for both the current year and the previous 5 years; the number of firms in the industry producing this particular chemical, and their aggregate capacity; the exports and imports involved with the chemical; and formulators and distributors of the chemical.

The international nature of the problem has become crucial in recent months, since the international export market has been much stronger than the domestic market. The relaxation of price controls earlier this year has helped to alleviate this price situation somewhat, but producers can sometimes obtain better prices overseas for many of their pesticide products than they can domestically. With expanding world food production, this could pose a serious problem to selected substitute chemicals experiencing increased domestic demand as well.

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*Economist, Economic Analysis Branch, Criteria and Evaluation Division, Office of Pesticide Programs, U.S. Environmental Protection Agency

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Figure 1

Mini-Economic Review Procedural Outline

I. Introduction
  A. Identification of chemical and nature (i.e., name; systemic)
  B. Broad use categories

II. Supply
  A. Domestic
    1. Production
      a. current
      b. recent five years
      c. number producing firms
      d. industry capacity (aggregate)
    2. Distribution
      a. number formulators and distributors
      b. location of same
  B. International
    1. Imports – volume, trend
    2. Exports – volume, trend

III. Demand
  A. Identify specific uses – agricultural
    1. Crop/pest combinations
    2. Geographic restrictions
  B. Usage
    1. Quantitied by crop/areas (regional, state)/years
    2. Acreages by crop/areas (regional, state)/years
    3. Identification of percentage of nationally pesticide treated crop
  C. Non-agricultural uses
    1. Use, area
    2. Quantity, area
  D. Efficacy and cost effectiveness (Agricultural)
    1. Physical effectiveness of alternative chemical
      a. indicators of control relative to check plot
      b. time frame of application
    2. Physical yield response
    3. Assess benefits and costs
      a. assign technical material and application cost
      b. value of yield response vs. check plot yield with 3 year average crop price
      c. calculate gross benefit

IV. Conclusions

In conjunction with the supply problem, the availability of feed stocks for pesticide producers may well continue to be a critical issue. With this in mind, the Economic Analysis Branch is expanding its expertise in assessing developments affecting supply and demand for pesticides as part of its overall responsiveness to the needs of the Criteria and Evaluation Division (C&E) of the Office of Pesticide Programs (OPP). We are in the process of data collecting, trade news monitoring, and generally conducting literature searches to assess the current and future supply-demand situation for pesticides.

Data sources to satisfy the entire supply section include U. S. Tariff Commission Annual Reports, U. S. Commerce Department Annual Reports, the Department of Agriculture reports, plus various agrichemical trade publications and sources. I might add that we have a fairly good working relationship with the relevant subbranches in these government agencies, and we are able to get at some of the disaggregated data.

On the demand side, this section can be divided into two general areas, namely use patterns and efficacy plus cost effectiveness. The first component is the descriptive analysis. All registered uses of the substitute pesticide will be considered. Data on quantities consumed are required to ascertain the pattern of chemical use and how it is evolving. This is required since many substitute chemicals are more target specific than the wider-spectrum pesticides they are replacing.

Information required for this includes the quantities consumed in pounds by use and area. For agriculture this would mean crop by region or state, if possible, plus the delineation of treated acreages by crop, region, or state. The information is needed for at least two points in time and preferably three to evaluate trends in the use patterns. This will indicate a replacement pattern for those chemicals which have been subject to adverse legal action by the Agency.

The other component concerned with efficacy and effectiveness is a design to further document the effectiveness of the chemical and its various uses, both major and minor. This is based upon available results of tests and literature. In the mini-economic review, the chemical is evaluated entirely without regard to other considerations. Later, under the Alternative Chemicals Program, detailed comparisons of performance can be made with specific chemicals subject to past cancellation in order to determine impacts on users and consumers.

So far, we have not included such comparisons in the mini-economic reviews, and a further delineation of this will be given by Dr. Aspelin in a few minutes.

The efficacy assessment step will be to evaluate the pest-controlling strength of the alternative in a pest body count sense or a percent disease control sense. This also involves consideration of a defined time frame of application and the length of time various levels of control are effected. Next, user costs are considered. The substitute chemical may require more pounds of technical material and may cost more to achieve some level of control relative to a canceled chemical. Again, we are looking at these chemical costs by themselves, however.

It is important to get a handle on increased cost of application to the farmer. The agricultural sector has a demand curve which is inelastic so that the farmer is essentially a price taker; he alone with his crop cannot affect price when he brings it to the market. He cannot readily pass on increased cost in producing his goods, unless, of course, we have a situation that has developed in recent years — well, the last 2 years to be more specific — in which the results of an exceptionally strong demand for more and higher quality foodstuffs both here and abroad have resulted. This strong demand has allowed farm operators to pass some of their increased costs along in the market, but history demonstrates this has been a unique experience and the future frequency of this is uncertain.

Data requirements here are rather simple. We need the cost of technical material plus a specialized application cost. If the pesticide is applied concurrently with the seed at planting or with the fertilizer application, it has been our approach that the application or placement cost is considered infinitely small and of little consequence to the analysis.

The last step brings together the first two in an assessment of gross benefits. Analyzing percentage kill data is not enough. It is only part of the pest control strategy of a user, since economic returns are his goal. We need to know the effect on yields and to translate that into evaluation of the product increase.

For example, we may have two test plots, one treated with the alternative chemical and one untreated. The positive difference of the former over the latter would be the yield increase; taking a recent 3-year average price of the crop in question and multiplying it times the unit of measure would give the gross benefits unadjusted for application costs.

The data sources for the yield response are EPA registration file data, state experiment station results, or other studies. The evaluation of the yield response is then compared to the cost of application, which will give a gross benefit as shown in Figure 2.

Figure 2

Gross Benefit Calculation

Value of Increased Yield From Treated Crop

— Material and Application Cost

= Gross Benefit

This demonstrates the substitute's effectiveness as an alternative to a chemical which has suffered adverse legal action from the agency.

This empirical conclusion then answers the question: Is there an economic substitute or substitutes, as the case may be, for a chemical which has suffered adverse legal action by the Agency? This is a yes or no question with no preference ranking of any of these substitutes. Whenever possible, as far as data limitations are concerned, this will be done on as many specific target crop pest combinations as possible.

The preceding works best for agricultural uses, but for industrial and urban uses it presents both conceptual and empirical problems. As an example, how do you measure the benefits of brush-free rights-of-way to the user? In the case of electric utilities, one of the major uses, it would simplify maintenance of electric transmission lines and noninterference from trees and brush.

How do you quantify these benefits? In those cases in which the benefits are nebulous and hard to define and quantify, we have suggested to our contractors and our in-house personnel to utilize an alternative costing strategy which considers non-chemical control. For uses such as home fly control, how do you quantify the probabl reduced health and nuisance costs, plus the obvious aesthetic benefits of not having flies buzzing around the home?

The alternative costing technique is viewed, then, as the best possibility of offering some economic input to the research process for these areas.

In conclusion, we would like to stress the initial first-cut nature of the mini-economic review. In many cases we are in a data-short position with respect to use changes in the last few years. Although three USDA nationwide use pattern surveys have been published, there is little available data on nationwide use changes since 1971. Efficacy data and yield response data are limited, especially the latter. One of our major tasks in the mini-economic review is locating new sources of data as well as interpreting existing sources.

BIOSPHERE REVIEW

Lamar B. Dale, Jr., Ph.D. *

The biosphere includes all living organisms interacting with the earth's abiotic environment. It includes all ecosystems, which interact within and among themselves to maintain steady state in both the flow of energy and the cycling of nutrients. The complex interactions which lead to this transfer of energy and nutrients provide for the opportunity of the transfer of toxic materials, such as pesticides and their metabolites.

Pesticides are dispersed in the air, water, soil, and moving organisms and can eventually be found far from their original source of introduction. Two types of impacts on the biosphere may result from this dispersion. One is the adverse impact on specific birds, fish, and insects that are vulnerable to pesticides and their metabolites. The second is a potential vulnerability to ecological processes as fundamental as photosynthesis in the oceans.

To assess these impacts, the biosphere review will entail a similar scrutiny of the literature previously cited for the initial scientific review. However, the detail and comprehensiveness of this review requires a total evaluation in quantitative terms, whenever possible, of the potential hazards of the use of the pesticide in question. An in-depth review of the current literature and consultation with experts in the pesticides research field will be required to compile this information concerning the current pesticide research by individuals and private academic institutions.

Before we continue, let me emphasize a point that came up several times this morning, that EPA not only has the responsibility of ascertaining that a pesticide does not produce an unwarranted adverse effect on the environment, but also has the equally important responsibility of not sacrificing a good, economically important pesticide without just cause.

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*Branch Chief, Metabolic Effects Branch, Office of Pesticide Programs, U.S. Environmental Protection Agency

Unlike the chemicals reviewed in the internal reviews carried out by EPA in the past and present, the pesticides that will comprise the alternative chemicals list will be selected because they are considered to be effective for certain uses of canceled pesticides. And, more importantly, they have been selected because they have been considered to be safer for the uses in question than a canceled pesticide.

The purpose, therefore, of the initial scientific review, as presented by Dr. Burkhalter, is to confirm this original appraisal. However, if the initial scientific review uncovers evidence that may cast doubt on the safety of the alternative pesticide, a biosphere review is initiated.

In this review, the area or areas of question will be studied in depth. In carrying out this review, we will not only utilize data studied in the initial scientific review, but also utilize data from studies in progress, utilize new techniques of data analysis in order to obtain full meaning from these data, initiate the development of new test methods which will yield more meaningful data, make in-depth studies of the exposures resulting from the use or uses involved, and only then determine if the risk is real.

If the risk is not real, we will have concrete evidence that the pesticide is a true alternative for the use in question, and we will be able to defend this position.

If the risk is real, the risk will be weighed against the benefits derived from the pesticide as determined in the socioeconomic review which Dr. Aspelin will cover.

By necessity, each biosphere review is unique unto itself. We will not know the problems we will be studying until they arise. Each review will present its own problems and the design of each study will be dependent upon these problems. Therefore, at this time, I can only speak in broad generalities and tell you what we envision.

I am going to address a number of areas of concern. Certainly, I do not have expertise in all of these areas. However, in addition to the Criteria and Evaluation staff, we do plan to utilize both industrial and academic experts and consultants to assist us with this difficult task.

I will attempt to answer three questions: Just what a biosphere review is, how we carry it out, and why we carry it out. I have already briefly touched on the answers to all of these questions. I will try to go a little deeper, or as deep as I can at this time, into the answers.

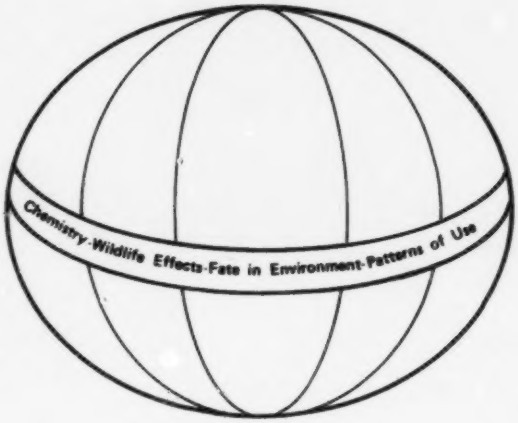
Just what is a biosphere review? Certainly, from the name it sounds as if we intend to study life itself, but actually, the study is not quite that ambitious.

First, the review consists of an in-depth study of the area or areas of concern as indicated by the initial scientific review. Secondly, the biosphere review attempts to relate any real question of safety uncovered to possible effects to man and the environment which may result from the use of the pesticide. In other words, we are taking the position that it is not enough to demonstrate that this pesticide in high doses produces an effect in a test tube or in laboratory animals; we will try to make an estimate of the meaning of this in real terms of human exposure.

The initial scientific review can be considered as taking a thin horizontal slice across the biosphere as follows (Figure 1). This includes the available scientific data on chemistry residues, toxicology, wildlife effects, fate in the environment, and patterns of use.

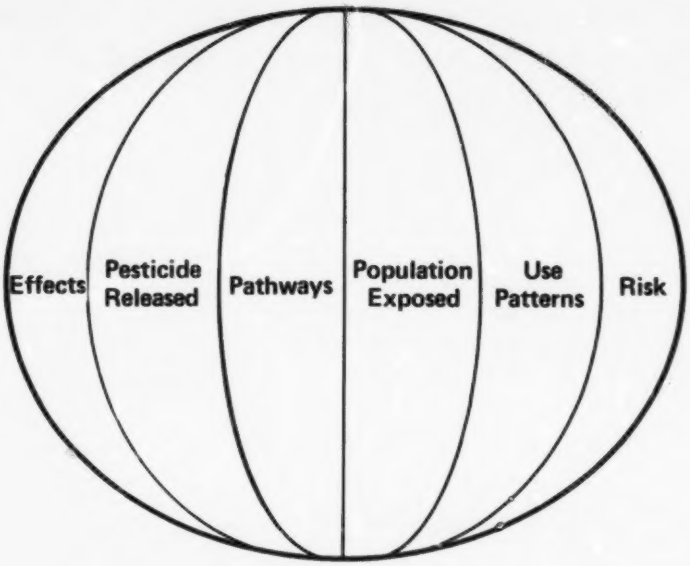
Figure 1

Initial Scientific Review


Chemistry-Wildlife Effects-Fate in Environment-Patterns of Use

In the biosphere review (Figure 2) we take a continuous slice through the biosphere and attempt to relate each slice one with the other in order to determine how one area affects other areas of concern.

Figure 2


Biosphere Review

Effects
Pesticide Released
Pathways
Population Exposed
Use Patterns
Risk

If in the initial scientific review (Figure 3) we uncover a question of safety in one of the areas of concern, we will first study that question area in depth.

Figure 3

Biosphere Review

1. Rereview of the study or studies in question
    a. Examination of raw data (and tissues) if available.
    b. Determination of suitability of species utilized.
    c. Subject data to other techniques of analysis.
2. Search for and evaluate other studies, unpublished or in progress, and
3. If necessary, design and carry out studies which yield necessary data.
4. Utilize these data in assessment of exposure effects.

For example, this may be a chronic toxicity. The first thing we will do is review the question study in depth. How do we do this? The first possible step is to reexamine the raw data and the tissues involved, if they are still available, and to submit these tissues and these data not only to our rereview but also bring in consultants for their opinions of these data.

In this we may determine if the species of animal utilized was the best species to demonstrate this effect and if the best analytical technique and the best statistical treatment were utilized. If not, we will try other techniques.

The second step is to search for other studies in progress or other studies which have not been reported. This we can do through the manufacturer himself, through academic institutions, and through research going on in the government. Then we can assess these data. If this is not enough, we can design and carry out other studies that would yield the data required to make a decision. Finally, after all of these steps have been taken, we will utilize these data in the assessment of the possible exposure effects resulting from the use of the pesticides.

The next step in the evaluation of the pesticide use is to determine the quantity of pesticide released into the environment (Figure 4). This release may be in the form of a controlled local release or an accidental or industrial loss. This will depend mainly on historical data obtained from industrial and governmental agencies.

Figure 4

Biosphere Review

1. Evaluate quantity of pesticide released into the environment.
2. Determine pathways of migration of pesticides.
3. Determine exposure resulting from use patterns.
4. Determine exposure/effect relationship between each use and health of man.
5. Estimate present and projected populations at risk.
6. Use estimates in conjunction with data developed in Socio-Economic Review to make benefit/risk analysis.

The release due to accidents will be difficult to predict, as scanty historical data exists. However, by resorting to data available in related fields of hazardous material, we will make transport and production estimates of expected release of pesticides due to accidents in industrial and transportation operations.

Once the current and projected release of a pesticide is known, we will determine its migration patterns in air, land, and waterways, as may be appropriate. We will track the most significant pathways by identifying organisms and their interactions which comprise transfer mechanisms. By estimating the amount of pesticide or metabolites lost or accumulated in each transfer, we can assess the level of exposure to vulnerable organisms or ecological processes. In addition, use patterns, formulations applied, and established agricultural practices will be examined in detail to determine human exposure as a result of application of the pesticide.

Having established migration pathways of the pesticide and exposure resulting from its application, we will determine the exposure effect relationship for man, animals, plants, and ecological systems identified as being vulnerable in the above study.

Assessments of possible effects will be obtained from the pharmacological and toxicological data reviewed and/or developed in this study. Based on all information developed in the study, we will estimate the present and projected populations that are jeopardized by a particular pesticide use and the degree of risk involved.

The information developed in this study will be utilized in conjunction with the data developed in the socioeconomic review to make a benefit-risk analysis for each pesticide use. This is a very ambitious undertaking, and, as I said in the beginning, all of these steps will certainly not be required in each case in which a problem is uncovered.

THE SOCIOECONOMIC REVIEW

Arnold L. Aspelin, Ph.D.*

I am most pleased to share with members of agriculture, industry, and academia some of our current plans for socioeconomic analysis in support of EPA's Alternative Chemicals Program. It is a distinct pleasure and a challenge as an economist to be a part of the Alternative Chemicals Program and to be here to discuss the role of socioeconomic studies in it.

As we saw this morning, the needs for data on economic and social values are great. While this is true, economists and other social scientists are newcomers to the analysis of pesticide matters, compared to our friends in the physical and life sciences.

What is a socioeconomic review? In general, it is a scientific review of the economic and social consequences of the use of a pesticide for purposes of contributing to the data base for determination by the Administrator as to whether the benefits of use justify the risks to be taken in the case of a pesticide which has been proven to generate risks if used as an alternative to a pesticide subject to past or prospective adverse regulatory action. The focus of this socioeconomic review is the expanded use of the pesticide as an alternative — not its regular, present use.

As Dr. Korp noted this morning, there are no easy, magic formulas to answer this question. Consideration of social and economic values in pesticide regulatory matters is mandated in FIFRA as amended in 1972 in the definition of unreasonable adverse effects on the environment, which is the prime criterion for decision-making under this law. It is defined to include any "unreasonable risks to man or the environment, taking into account the economic, social, and environmental costs and benefits of the use of any pesticide."

Detailed socioeconomic studies which cover the several areas cited in the above definition are undertaken only in instances in which there are some

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real or proven risks to man or the environment due to the expanded use of the alternative which could conceivably be justified on the basis of social and economic benefits. In such a case, economists and other social scientists conduct studies in a multidisciplinary mode, interfacing with the physical and life scientists who conducted the biosphere review.

One is struck with the scope of the definition of "unreasonable adverse effects" on the environment, bringing with it the possibilities for excessive amounts of analysis leading to a burden on program resources and a lack of timely decisions under the program. But this will not be the case. As you would expect, the analysis of social and economic values is being implemented in OPP without an excessive budget.

Let me hasten to say that it is not without an adequate budget. With the possible exception that we need many critical data that are not presently in our hands in order to achieve our task, there are many critical data needs which require further exploration by all groups interested in regulatory matters.

Let me make one more observation before turning to the components of a socioeconomic analysis. The concept of "unreasonable adverse effects" is not a precise term. It provides for flexibility under changing economic conditions and national priorities such as has been necessary during the energy crisis and recent pressure on food supplies.

A unit of environmental protection is much more expensive today than it was a year ago. It's likely to become more expensive in the future. Fortunately, Congress has not hemmed EPA in with fixed coefficients in FIFRA, such as was the case under the Air Act, where you had to have 90 percent reductions according to the law, regardless of cost.

I will now discuss the various components of a socioeconomic analysis in general terms as we presently envision conducting such an analysis. At the present time, we have not conducted one. We have not made plans to study any specific pesticide as an alternative along the lines of the framework being discussed today. And maybe we will not need to conduct one under the Alternative Chemicals Program.

Throughout my discussion, please keep in mind that we are thinking in terms of a time horizon for a socioeconomic analysis of approximately 5 years corresponding to the time period for which your registration is effective under FIFRA before it would need to be renewed. It remains to be seen whether it will be feasible to thoroughly study a future 5-year period because of limitations on data and available time to conduct needed analysis on the basis of 5-year projections.

The first step of a socioeconomic analysis is a review of the production and distribution system for the pesticide, its registered uses, associated patterns of use throughout the country, and data on application methods and rates. The next step is to project use of the pesticide crop by crop for other use over the time period covered by the study, based on demand and supply conditions. This evaluation will take into account cost effectiveness of the pesticide in competition with the problem pesticide and the size of the market for use of the pesticide. On the supply side, attention will have to be paid to technical and economic feasibility of producing and distributing the pesticide in needed quantities.

In short, can industry deliver the product and will the farmer buy it? The projections of use during the period covered by the analysis are critical, because without them it is impossible to make realistic assessments of the nature and magnitude of economic and social benefits. Such projections of use are also necessary for projecting populations at risk and making estimates of total effects of health and environmental impact, as has been discussed under the biospheric review.

This section on levels of use would be done jointly by the economists and the scientists involved in the biosphere review. The evaluation of economic benefits is divided somewhat arbitrarily between primary benefits — that is, those for which the pesticide was purchased by the user — and those which are secondary or of a by-product nature.

In the evaluation of benefits, we will be estimating the addition to goods and/or services attributable to the pesticide over and above that which would be obtained without the use of any pesticide. We may also compare productivity of the alternative to the problem chemical.

In this analysis, we are aiming for data which will help the Administrator or other decision maker to determine whether the alternative is a step in the right direction and/or, further, whether it generates benefits which justify the risks. It is possible that an alternative does not generate benefits which justify the risks even though it is better than the problem chemical. In such a case, we would need to look further for an alternative.

The evaluation of costs is quite straightforward in the case of primary costs. However, the secondary cost estimation is much more complex as it covers the unintended and unavoidable cost to users, other parties, and the environment based upon the results of the biosphere review. Here we will evaluate in economic and social terms the positive and negative side effects of the use of the pesticide. It is obvious that this will be one of the most difficult areas of analysis in a socioeconomic review. This part of the analysis will depend heavily upon estimating exposure/effect relationships as discussed earlier by Dr. Dale or as developed in connection with the socioeconomic review.

The social impact analysis area is just now being charted in our office in terms of the areas to be focused upon and the types of analysis to be conducted. At the present time, other agencies are active in the area of integrating social impact analysis into program criteria and implementation. Our major effort here will be to determine the importance of the pesticide to identifiable groups, communities, and institutions and to determine what effects will occur if the pesticide is vastly expanded in use as an alternative, including demographic factors.

The social impact analysis is likely to be of greater scope in instances in which the pesticide is of controlling importance in determining cropping patterns and geographic location of production, such that its use would prevent major economic dislocations and attendant social impacts on families and communities.

We are not expecting the socioeconomic review to ultimately reduce itself to a naive textbook benefit-cost or benefit-risk ratio, but rather offer indications of the nature and magnitudes of benefits, risks, and costs upon which to judge whether a pesticide is economically and environmentally acceptable as an alternative to a problem pesticide.

DR. AXELROD: I wish we had a few minutes just to sit back and think of what was said and shown here. And, in a very pragmatic sense, and, hopefully, a very objective sense, anticipate if these kinds of studies, scientific and socioeconomic, were instituted years ago, would we come to many of the litigations we have today? Would we be able to iron out difficulties, some of which Dr. Whittemore discussed this morning, but not as witch hunts, but where we could delineate the problems, bring them to the manufacturers and have them work out the problems before the babies are thrown out with the bathwater?

I think we should, throughout our discussions, rather than perpetrate adverse reactions or adversary approaches to these new studies and new looks at these studies, anticipate what benefits rather than risks at least the industrial sector would go through if indeed such data bases were developed. Such analysis should really develop before important Agency personnel would sign off on cancellations, suspensions, or other adverse effects in which the adversary approach becomes the master of the situation rather than the scientific, economic, or social aspects.

QUESTION: I was most interested in your economic assessment. I think this is very commendable. I know nothing about economics, so I can speak with some authority on the subject, and at least ask an intelligent question.

In your analysis, it looks like to me we're talking about rather an idealized situation. There are two things that sort of concern me though, and I wonder how you're going to deal with these. One is the current situation that we're going through of an energy crisis. This has had some impact on the production of agricultural chemicals. I get various numbers, but, for example, one group tells me that they are unable to meet their customer demands for phenoxyherbicides. They can only meet about 60 percent of these. How would you deal with these kinds of crises? Can you handle these in your economic considerations on a long-term sort of an approach?

The second question that concerns me, and it really shows my lack of knowledge about economics other than what I see on NBC news, but there is this. What you say is true about the farmer not being able to go to the market and pass off his costs to the consumer. But it appears that the drought is going to have some effect on crop production. And the numbers stick in my mind something like the corn yields are down 10 percent and soybean yields are down 13 percent. And this will probably change by the end of the year.

But one aspect of this was that this will be passed on to the consumer, in reality, in the higher feed grain costs, in the higher meat prices. How can you look ahead this far in your proposed cancellation and substitution of new chemicals to determine how this might affect the American consumer? And this could be a very adverse effect.

DR. ARNOLD ASPELIN: Economists have conducted extensive evaluation of the impacts of changes in technology, weather conditions, and other factors such as you indicated. Economic models and theories and most needed data are available for such things. The problem is the degree of precision.

It isn't much satisfaction to the policy maker who has to go ahead and make the decision anyway that there are problems in making estimations of such impacts. So we have to make the best use of the available economic theories and data in generating information on what these impacts will be to be taken into account by policy makers in pesticide matters.

Some of these costs will initially stay at the farm gate, but eventually they will shift on to the buyers of intermediate products and the final consumer. It sometimes takes quite a while for some of these things to work themselves out through the economic system.

As far as the energy problems are concerned, there are an awful lot of unknowns in that area, too. As Jeff indicated, we are making intense efforts to assess the market conditions in the pesticide chemical supply industries, as well as in the demand area, to determine how critical shortages might be, impacting on 1 year down the road and even looking farther on.

MR. JEFF CONOPASK: I'd like to address the second question. That is a very difficult problem and it gets basically to the problem economists have with some of the sophisticated models that they do develop. We can only answer certain questions. We hold many things constant in an attempt at answering certain questions. We can't anticipate everything.

I might take an example from a Corps of Engineers study that was done a few years ago for a dam in Pennsylvania. The Corps, innovative as it might be in some of its long-term projections, assessed the possibility of a large flood in this particular valley. They had what is known as a once in a 100-year lifetime flood. And they gave some probability and they used a very, very sophisticated systems analysis to assess this. Well, it so happened that in the second year of this project, that 100-year flood hit. So, how can you predict this? I'm just, you know, perhaps second guessing ourselves here. But we just don't know some of these things. And it's very, very hard to predict 5 years into the future, let alone, 10 or 15.

DR. AXELROD: Fundamentally, some very shocking decisions may have to be made on a temporal basis. Ones that no sector sitting here would immediately accept. Nevertheless, decisions will have to be made on the basis of impact on this country, to wit, the recent energy crises. Suddenly, a reassessment of priorities occurred to extents that we didn't think possible. Nevertheless, these modifications of our lifestyle or perhaps our feeding habits will occur. It depends on the severity and the longevity of these adverse effects and impacts on our society.

QUESTION: Would you anticipate that research would begin along use lines? That is, looking at equivalent substitutes for a given use or throughout general substitutes. In other words, replacing DDT, replacing deildrin, replacing 1080 with the top substitutes for each of these chemicals or looking at the five substitutes for DDT or five substitutes for deildrin or five substitutes for 1080?

DR. ASPELIN: Focusing research on uses makes sense from the economist's point of view because that's where the benefits lie. And this would be helpful, but we don't want to completely focus on uses. I think it would be helpful to, on a priority basis, allocate research on the basis of uses. Priority should be given to uses with the most hazardous pesticides, the most intensive pesticide use levels, and those with the fewest or most limited alternatives to problem pesticides.

MR. CONOPASK: One thing to add to that, again our resource problems — it may be difficult to uncover critical minor uses and I don't have an answer to that question. There may be some uses that are very small in the agricultural sector, let's say, which are critical, and yet don't have adequate substitutes. Hopefully, we can locate these with our resource funding level at the present time.

QUESTION: As I understand it, the biosphere review and the socio-economic review won't be conducted unless a problem shows up in the initial scientific review or the mini-economic review. These initial reviews are going to be following along the lines of a registration review, using the same criteria? In other words, if a person has the information package up to date, as if he was currently registering a product with the initial reviews, does this not go beyond those requirements?

DR. AXELROD: Certainly, information from the jackets and from the registration division will be utilized in that initial scientific review with a prime focus or foci on those mountain tops we discussed. But the initial scientific review does not relate to an original registration.

It should be stated here that an inordinate number of registered pesticides obtained their registrations many, many years ago. Those that have registered in the last few years are quite different contextually in the areas of initial scientific review data bases from those that were registered 25 years ago, which constitutes some of our major DDT substitutes at this time, just to take an example.

So contextually it will include all the data bases that we have, particularly those in the registration division. But as Dr. Burkhalter pointed out, there is an overview review containing all those points that he discussed in his brief outline of the initial scientific review. It's to bring up any major point of contention that may find its way into an in-depth review in the biosphere.

Now we have reviewed a few compounds thus far. It should be stated that this entire program was only resource committed March 1 of this year. We couldn't regress into the suspect chemical review. We had to develop a new thrust of benefit concepts, a broader base than immediately obvious suspect problems, which is part of the internal review.

So to answer your question, at least in part, those data bases obtained from the initial registrations will be utilized. But depending on what data bases have developed since, they also will be utilized.

QUESTION: Could a good start for a data base be the requirements for registration as being proposed under the guidelines?

DR. AXELROD: Absolutely. Particularly under the present guidelines, which should come out in November '74.

DR. DEAN KATSAROS: I'd like to know how much thought you've given to how you're going to arrive at this cost figure. In each instance that you will be considering, you'll be talking about an increase in production over what's currently being used, because you're going to replace another material. And you'll be asking questions that even many of the chemical manufacturers don't know the answers to. If you're going to replace a major pesticide use, you may be talking about a very substantial increase in volume.

DR. ASPELIN: To pick an example, we might find that a pesticide that accounts for 90 percent of a use all of a sudden comes into question for cancellation. Further, let us assume that the remainder of the use is covered by a pesticide which is being considered as an alternative to that canceled pesticide. The immediate question is "How much of the void created by a cancellation could be picked up on an economically and environmentally acceptable basis?" think the government and industry and academia have a joint responsibility in looking at such issues.

I think as a normal course of business, a firm will be looking to expand the market for its various products. This represents not business as usual, but an opportunity to the industry to expand the use.

And, further, let me say that a pesticide which is economically and environmentally more acceptable than another one should command a premium in the market. I really think there's an opportunity for industry and government to join hands here and make it go.

DR. AXELROD: Someone once taught me way, way back in an introductory course on economics that there is a supply-demand concept, and that if one can expand the supply to the demand, prices usually go down. This may have nothing to do with our present economic situation, but I think that that is one of the supply-demand rules that they teach you in Economics I. I don't know if it's real.

QUESTION: Along this very same line, let's assume we're under a very extreme situation where you have a compound that's on the market today that costs the grower 50¢ an acre to use and that is canceled out, and the only alternative product that is available for that costs the grower $10 an acre to use. But because of your survey, you just wouldn't be able to make that recommendation. You just couldn't justify accepting that kind of a spread in economics.

On the other hand, if I had your endorsement of my product, which costs $10 a pound to put on, I could then expand my production and put it out for $5 a pound. This might be within the realm of acceptability. What do you plan to do? What is your program in regard to working with products that are in small production or new production for which the price is at what we might call a development price, as opposed to a product that has reached maturity and is at a much lower price? Are you going to throw it out because of that? Or have you even thought about it?

DR. ASPELIN: Well, as I indicated, there would need to be an analysis of the potential for increasing the supply of the product. And this is going to involve looking at the impacts on cost as you increase the quantity. It may well drop from 10 to 5 to 4 to 3 to 2 to 1. It may, as you increase quantity, also drop the second year after you go into production. Or maybe the best available control is considerably much more expensive, and if there simply are no alternatives and the market will not stand for the use of the $10 compound, you're going to have to result in no use and the price could conceivably have to go up to the consumer.

If there's no way that the farmer can afford to pay the $10, the product is obviously going to be produced without it. Now, hopefully, this will never be the case. The impact on the consumer will depend on how important that $10 is. If the $10 per acre compares with the total production cost of $200 an acre for the product, there would be a fairly nominal increase in the cost on the market of the delivery product.

On the other hand, if the $10 is half of the cost or something of that sort like it might be on wheat, it would be very substantive. But hopefully there will be economic alternatives within a near range in cost to the one in question.

QUESTION: Would you anticipate that a substitute chemical might be completely acceptable from all standpoints except economics and would be thrown out on the basis of economics?

DR. ASPELIN: We would not throw it out on the basis of economics. The realities of the market in which it's used will make the decision. If the best the industry can do is $10 on the cost of the pesticide, the market is going to have to determine whether it can justify its use. In other words, can the input market that the farmer is in justify using it? If it doesn't return $10 plus something else, he simply won't use it and you'll produce the commodity without it.

DR. MORRIS CRANMER: If we could get away from perhaps the production costs in this economic equation for a minute and think about the health effects or just the effects costs of providing equivalent data bases for making some of our decisions. I believe Dr. Axelrod directly referred to the fact that different types of data bases are available for different compounds which have been used.

As a generalization, compounds in heavy use and in long use have a larger amount of effects data accumulated on them. I would think that we would, in making this type of decision, want an equivalence of comparisons, and is it included in the analysis and economic determinations of how much it would cost to go through these machinations with various other compounds?

In other words, in your cost assessment analysis, do you determine how much it would cost to generate equivalent health and effects information on the several candidate compounds that might be considered as replacements?

DR. ASPELIN: As I indicated, the socioeconomic review would attempt to evaluate the costs of avoiding health effects, the cost of treating health effects, and this would be at the levels of use of the pesticide that would occur as a substitute for a canceled compound.

We would be doing these comparisons with the pesticide that's being canceled more or less on a one to one basis to see whether we're going in the right direction. But you can't limit your concerns to one particular area. It may well be that it will be very expensive to develop the necessary data, to evaluate the significance of health effects in economic and social terms. But it's going to have to be done, and it would be done in such a way that you would know whether you're making a step in the right direction as you go to the other compound.

DR. CRANMER: It occurred to me, perhaps not being as familiar with the subject as you, that in order to make your long-term assessment of health effects,

effects on the human population, one would have to have equivalent data bases to make that projection from. And, since biological information — for instance, the toxicological information data bases — will be dissimilar for the various compounds, in order to make an equivalent projection, you would need to at least adjust these data bases.

And this might be sort of an early process, I would think in my own mind, prior to the time of getting into some probability assumption of costs of future health effects of a compound that we have insufficient information on.

DR. AXELROD: I don't quite follow part of your discussion, Morris. If you have a pesticide which is useful on 10 acres, are you proposing that we obtain equivalent human health effects on that as we would commit resources for something which is used on 100 million acres?

DR. CRANMER: No, not at all. That's one of the easy parts of the equation. Let's say that you have approximately equal projected usage rates in usage areas, but you have a dissimilar toxicological information base from which to make your projection.

DR. AXELROD: This is going to be presented by Dr. Buckley tomorrow, because he sets into place the data base retrieval possibilities for human health effects, as well as other ecological ones. And he will have to assess the priorities of which goes first for the resources committed in retrieving such data bases so that Dr. Aspelin can make the right economic assessment.

DR. R. E. HANSON: One could ask: When you get this data base, $5 million looks like a very minimum amount of money, yet when I hear the programs, that is exactly what you're talking about — if you had $5 million and you get another $5 million for '75, that is if you're lucky. Or is that already committed for 2 years?

I mean, addressing the question that was just asked about bringing things up to data bases, I mean, two toxicology trials, for instance, if that's one of the data bases you're looking at. I don't know — $65 to $100,000 per chronic trial. Five million dollars goes pretty fast.

DR. AXELROD: The equation, of course, relates to not overstepping what resource commitments you need for the number and type of substitute chemicals you study. I mean, to take it out of perspective is an exaggerated situation. You wouldn't take one chemical compound and commit the $5 million in research for that compound. You would have to assess on a variety of levels the proportionality of commitment.

Now, I don't know particularly what your thrust is or what your answer is to what you're asking, because you ask your question with an answer behind it, and the answer is in your mind. But in government you kind of live day to day. And you sometimes reassess your priorities every hour. And all you can do is try to rise to the occasion and to assess the needs of the moment and address them. And then, what happens tomorrow, little things like vetoes on appropriations bills, you deal with as it comes along. It's good in two directions. First, because it gives you flexibility. Second, if you don't act that way you get nothing done.

And the real name of the game is to get something done and get it done in as good and as contributory a fashion as possible — scientifically, economically, what have you. I think it was very important that it was brought up that whatever decision is made, whatever policy is formed, that was today. Five years from now, it may be completely different, or 5 months from now it might be different.

Decisions were made a few years ago that we're still living with, still trying to understand. So, the name of the game in government is rise to that occasion and keep plugging.

But I feel that we have a 2-year commitment to a program. We've assessed what portions should be studied, where the money would go best. We get the best data retrieval to serve not only government, but the industrial sector, so that they can have a better appreciation of where problems may be found if resolved by their efforts in research and development on a much broader base than perhaps they can look at themselves.

QUESTION: Manufacturer of compound B takes 2, perhaps 3, years before he expands capacity to be able to take over 100 percent of the market. What do you do on compound A during that 2- to 3-year period? Do you give a temporary extension of its registration for 2 or 3 years until the other one comes in, or do you cancel it now and leave the farmer without pest control for that 2 to 3 years?

DR. ASPELIN: Obviously, this type of a trade-off in terms of time needs to be considered probably a lot more than it has been in the past. There are some options for the timing on these things. The all or none and right now type of decisions are very expensive.

And, as we all know, markets take time to receive signals and to do things to make adjustments. Instant changes, instant cleaning up of the environment, is very expensive. For some of these decisions, the sooner the better, obviously. But maybe the cost isn't worth it that quickly. So there are trade-offs through time that should receive intensive policy type analysis.

QUESTION: Is there coordination between this program and the other divisions so that cancellation occurs at the right time?

DR. ASPELIN: You're getting over into the policy area, which is beyond the economics, but there does need to be this type of policy analysis at the end of the kinds of comprehensive analyses in the various areas that we talked about today.

DR. AXELROD: One of the major thrusts, though, of the Office of Pesticide Programs is to synchronize the efforts of the Registration Division, Criteria and Evaluation Division, and Technical Services and Operations Divisions. And it's a new office. The divisions are new. This is not begging the question, but it means that there are many roads ahead of us in which requirements for genuine synchronization of efforts and decisions at other levels will have to be done.

DR. JERRY SMITH: In the economic equation, are you considering only domestic economics, or are you considering international economics as well and the effect of changing any cost to the farmer in his ability to compete internationally?

DR. ASPELIN: I think Mr. Conopask alluded to the fact that we indeed must consider the impacts and the realities on an international basis, but we start out working at the middle of the problem, which usually is pretty close to the farm gate. And we work out from there. But we do have to recognize the international implications of what we do, and the implications of things that are happening elsewhere in the world. But we're not on an island, economically or any other way. And this is an important area of inquiry and we will not forget it.

DR. AXELROD: I think it's important to state that you all have many questions and, believe it or not, we don't have all the answers. The stimulus you give us in these areas of questions will be addressed. They are not a matter of verbal pitter-patter. They are a matter of deep concern to us and to the Agency. These questions stimulate many issue papers which will be developed in the Office of Pesticide Programs.

It is the beginning of a program in a positive sense to help. These questions, and, hopefully, some forms of answers that we can derive over the next few years will help in that decision-making and in the policy-making of the agency.

MR. ALFRED MITLEHNER: In line with what you just said, I won't ask a question, but I'd like to express two points of concern. One is, from the point of view of the socioeconomic review that's going to look 5 years ahead, I find it hard to understand how such a review could be meaningful if this does not include the introduction of new compounds, particularly those compounds very near registration. It seems to me that it is these compounds or potential products that will have the greatest effect upon what happens in the marketplace.

Secondly, a very mechanical problem. I am very concerned that file jackets do not find their way into this initial review process and are excluded or lost from an ongoing review of a current registration request.

DR. ASPELIN: Let me respond to the first question. We will not ignore any significant factor affecting the demand or the supply for a substitute pesticide in the course of the evaluation of its potential. And if there are alternatives that currently are not registered, but are likely to be registerable down the pike, this is not the focus of the program but we will not ignore these things if we can develop scientifically valid data as a basis for taking them into account.

DR. AXELROD: We've gone through this exercise of making sure that those jackets are never taken out. That's the beauty of the Xerox machine and the beauty of Dr. Rogoff's capacity to overview the situation and very careful attention to trade secrets, to confidentiality of data, and so forth.

DR. G. W. PROBST: We've heard much about mini-reviews, mini-economic reviews in a system of phase one and phase two for evaluating pesticides, which, to me, is a model of thinking and planning rather than a reality situation. I would like to address one question. We are attempting to establish criteria for substitutes or alternatives to the so-called suspect chemicals. Don't you think it might be wise to select one of the suspect chemicals and check it through the proposed model and determine how a suspect chemical will fare? It might fare pretty well — including in a socioeconomic situation.

DR. ASPELIN: You're saying take one of the suspects we have and . . .

DR. PROBST: Test the model.

DR. ASPELIN: And test it in this type of socioeconomic study model.

DR. PROBST: As I understand, this has never been done. Is that correct, Dr. Aspelin?

DR. ASPELIN: We have not conducted the comprehensive review of the sort talked about in a review mode. Obviously, considerable amount of data have been generated.

DR. AXELROD: As a matter of fact, even in the internal reviews, until very shortly, to just a year ago, the requirement for socioeconomic studies was not part of the review process. It has been locked in by law, and the development of Dr. Aspelin's branch has been a very recent evolvement in OPP. Without asking for extra money, we're going to do that. Not going to talk about it much, but we're going to do that and see how it looks — might be very interesting.

QUESTION: I certainly wouldn't be one to be defending or saying anything about DDT, but that might be an interesting one to send through the economic review, particularly with the disagreement between the hearing officer and the past Administrator of EPA it might have an interesting result. Aren't you reviewing that anyway?

DR. AXELROD: As a matter of fact, the legislators have asked that the Agency review the scientific basis for the Administrator's decision, taking into account the social and economic consequences of the decision. And I think that gives you an answer.

DR. EDGAR TURTLE: I don't think it's specifically a question I wanted to ask, rather more in the form of an observation. I heard one of the reviewers, when talking about possible cancellation of registration, looking at the position of the manufacturers with their supplies and calling into his calculations the fact they might be able to sell their materials abroad.

I might say I, in my present seat, am looking at this discussion from abroad, namely, the repercussions abroad on the actions taken in this country. And I think perhaps DDT is one example there. There tends to be an assumption here. The statement "Well, manufacturers might not be so badly off, because they can sell this stuff abroad" was the sort of answer which was given to our manufacturing question.

Now, it seems to me the same thing works the other way around. That was just to meet the first year or so because the manufacturer has got some material on hand and he wants to get rid of it. There has been a cancellation of registration. He can sell it abroad and these people overseas, therefore, benefit from it.

But 3 or 4 years later, because of this cancellation of registration, the cost of this material to any purchaser depends upon the amount which is manufactured. Therefore, the person abroad, who now wants to get it, because your decisions don't directly affect him has to pay a lot more.

Now this may be a pesticide which is used, for example, in vector control, which now is going to cost a lot more. The only point I'm making is that in your socioeconomic assessments, could I make a plea that you at least cock an eye on the effects overseas, on these facts perhaps from a humanitarian point of view, not only from the point of view of how much more profit the American farmers will make or the American manufacturers will make? What are the effects on overseas in a socioeconomic sense?

DR. AXELROD: It's well put, Dr. Turtle. I think that Jeff Conopask and Arnold Aspelin both more than alluded to the fact that when people are making decisions based on socioeconomic studies, a good portion of them will address the international question.

I also think, personally, that in the light of humanitarian work, if we were to take a recent past example of DDT, I don't know that the use of DDT for human health, which still is on the books in the United States and in the world, if the cost of that should be borne by society, by international organizations with stipend or supplementation. There are very many questions that your question brought up as to how to handle, on an international basis, compounds which in an affluent American society, the United States, has seen fit to deregister or cancel, that the requirements for the American scene may be different from the requirements on the international scene in emerging countries, where they are more worried about tomorrow's breakfast and if there's going to be one, than whether they are going to suffer dire consequences when they're old. I think this is part of a very basic question as to the position the American EPA has on the international scene, both from its impact on decisions that are made at EPA, and also on the conscience of international organizations as to how they handle these things where there is a question of humanity.

MR. CHARLES KRISTER: I was hoping that the two gentlemen from the international agencies (WHO and FAO) would also make the same sort of plea to some of our European counterparts when they take their actions. There's been a tendency on the part of some of the countries to take very precipitous action in connection with certain suspensions or cancellations. Perhaps they too are setting a pattern which is undesirable.

I'd like to ask another question, perhaps of you or Dr. Korp, and put it in a little different light than Mr. Mitlehner did. With all this planning going on — mini-reviews, internal reviews, substitute chemical reviews, etc. in the Agency, what impact do you expect this kind of activity to have on registrations and in your tolerance clearances for new products or for additional new uses for existing products?

DR. KORP: Well, first, I don't think that they're unrelated, but I don't think that it's going to negatively influence the registration process. In other words, our procedures there will be to accelerate the process to do the very best we can to get answers back promptly and quickly, using these guidelines that Len now has promised for November, and, as I say, so the inputs will go back and forth, there's communications. But I don't think that you're going to have this program influence the registration program.

DR. AXELROD: In a positive sense, the good that can come from it is that we can have a much sharper, realistic approach to criteria for registration, criteria for the positive side of looking at registration.

QUESTION: I'd like Dr. Dale to expand on his comments that there's some sort of a tissue review. What are your guides? Would you explain to me about that?

DR. DALE: I didn't say specifically there would be a tissue review, but, for example, if the question of safety hinged upon a study which was based on a histological examination of a slide, say, hepatoma, we would rereview these slides and determine if, indeed, by using experts in the field of pathology, this is really a hepatic carcinoma or not, if the slides are still available.

In other words, going back into the original study in greater detail than merely reading of it in the initial scientific review and reviewing what has been written about it, going back and looking at the raw data in depth.

QUESTION: I am currently aware that manufacturers are not required and have not the volume of tissues or slides for a review by EPA.

DR. DALE: They have, in some cases, provided slides when there was a request. Not routinely, no.

QUESTION: Could I ask whether or not they anticipate that this would become more of a formality in the future, particularly with regard to registration of new products that they indeed would be looking at tissues and the slides?

DR. DALE: I think in regard to certain types of pathology, simply better record-keeping.

DR. AXELROD: I think it's a matter of intensity of need. In the usual registration process, data is brought forth. On the basis of that data, decisions are made at the registration level. Later on, perhaps, in a case of suspect chemicals internal review, you have to take a much greater in-depth look. Either you expedite new studies to assess lesion, or, as Dr. Dale puts it, the privilege of a number of experts looking at the original slides for diagnosis.

And this is a very real possibility. I think that we have had excellent cooperation from some industrial sources who saw fit to have confidence in their own expertise, who made decisions concerning lesions of various sorts. And this visibility is one which is not only justified, but is heartily acceptable to those who are trying to assess in a scientific fashion the credibility of a former decision.

We all know that particularly in pathology it's very hard to get two pathologists to agree. The best you can do is get a concensus of opinion, and that sometimes looks like that animal that's put together by a committee. That's what we're trying to stay away from.

I think I'm right by saying the way those slides were given is, you know, people get into an adversary hearing and then slides come out of the bags. And a lot of time, a lot of money, and a lot of manpower is wasted. Those slides could have gone into the hands of scientists to begin with, and, hopefully, a decision could be made that you wouldn't need an adversary hearing to determine in an adversary way whether that science is right or wrong.

QUESTION: Two questions: One, has the proposed program as outlined here been reviewed by the Office of General Counsel in EPA particularly to evaluate it in terms of the liability of the participants in case of recommendations that came out of the program that later were shown to be obviously wrong?

And the second question: There have been a number of references made with respect to safe, safer, during the discussions. How do you square these with the prohibition in the statute and in the legislative history, with respect to essentiality?

DR. AXELROD: What you're saying in the first question is "Is every decision made in the Registration Division, based on data forwarded by registrants, reviewed by the Office of General Counsel to determine whether that reviewer is liable for his decision?" Practically the same parallel exists when scientists are asked to make decisions on the basis of the best expertise knowledge and consultation with others in the field if they make a decision which later on proves wrong, whether one goes back and decides on double indemnity or liability of his decision-making process.

I presume that none of us here in this room have been without error in their lifetime, and I think your question is peculiarly biased as to this program, because scientific decisions are made every day in various aspects, and they're not unique to EPA or unique to the field of agricultural chemicals. There will be errors made. But the best defense you have against error is careful, scientific, expertise decision, not an adversary approach.

QUESTION: The reason for the question is that this is a new program within the Agency, as I understand it. It's a new approach. And other decisions within the Agency are certainly subject to different types of legal appeal, all of which are set forth in the statute.

My question is not with respect to an individual decision of this particular program, but whether or not the Office of General Counsel has looked at the program as a whole to evaluate it from a legal standpoint.

DR. KORP: The program was put together by OR&D and OPP. It was reviewed very thoroughly by OPM, which is a planning and management group, and I'm sure they have a General Counsel view. I think they're thoroughly aware of the program.

DR. AXELROD: It has also passed what is called the tenth floor. That is the OWHM which is loaded with lawyers who have made many comments on the basis of some of the things you're discussing. And long before you saw it, those things were either enlarged upon or removed. There are four lawyers up there who went over this program before it was sent to you or anyone else.

I don't know if that's sufficient unto itself, but it comes under purview of the same type of thing as the internal review or the registration review. It's a new slant. Hopefully not as an adversary approach, but as a constructive one. Nevertheless, it's a new program.

DR. AXELROD: In answer to the second question, I think earlier in our discussions I brought up the fact that words like adverse, unreasonable, and safe, are subject to all the subjective enunciations of biases of people. And we're all people, scientists or otherwise. And we do have one very important thrust contractually to delineate definitions, definitions of various words thrust upon us by the new FIFRA, such as unreasonable adverse effects, hazard, imminent hazard, risk, benefit, made by good legislators but perhaps without the need to delineate meaning to these words, leaving it to us. We are in the process of getting the legal, medical, social, economic, and other definitions of these words, hopefully, to more objectively utilize these words and their meanings in constructive decision-making. We all recognize how faulty a word "safe" can be.

Now, at the extremes of any equation or curve, it's simple. 10,000 people die of something, it's not safe. The question of whether six people dying out of so many is safe or not, that's a matter of risk and benefit analysis that really reverts back to enunciation of safety or not. We are very much cognizant of the risk one takes in enunciation of what safety or hazard or unreasonable or just adverse effects means, and we're studying that problem.

QUESTION: I'd like to refer back to a comment you made this morning, and maybe it's also related to what you were just saying, but you indicated this morning that the internal review process on a material begins at such time as there are concerns raised that you begin to study the problem, which may also then get us into the alternate chemicals review.

My question is, specifically: When does the noise level become high enough so that you begin and what are these various types of criteria? The accidental spill yesterday in Yuma — is this a type of thing that is a factor?

DR. AXELROD: That question, I think, is somewhat out of sequence. We will discuss what initiates the internal suspect chemical review, but the part that you said leads to substitutes, that doesn't lead to substitute chemicals reviews. Very pragmatic aspects lead to my being impacted upon for an internal review. For example, Dr. Korp says, "You will review this." Now, you may not think that's a good answer, but I consider it an excellent one. Or Mr. Agee says, "Dr. Korp, you will have Dr. Axelrod review this." It's a very good answer. And that's serious, because it isn't a matter of that good saying about "Ours is not to reason why," but, nevertheless, these people are impacted upon by various situations, some of which are just, frankly, political.

A couple of senators say, "You better make a review. We think this is a terrible compound." It becomes impacted upon the various levels above me, and somehow it filters very decisively into my division and we're making a review.

So, there're various reasons, various accusations made, various questions asked by many sectors — political, Congressional, environmental groups, etc., which come down in the form of "Lenny, you will review this compund now." And I really can't give you a better answer, because that's it.

QUESTION: I just want to make a comment, rather than pose a question. It seems to me that in this whole review process, science will best be served if we can keep this on a scientific dialogue through much of this review process. When it becomes legal, things get tough. You know what I'm talking about — recent situations that we've had that when the legal arm moves in, dialogue dies. And I'm sure that you're going to think about this in your overall matrix system, but the protagonist and the antagonist can speak freely and argue scientifically and trade data and call each other on the telephone, and send papers within the constraints of the Agency. But I'm also aware of some experiences we've had that when the legal arm moves in, this sort of dialogue dies. And I would hope, speaking as a scientist, we could keep our channels of communication as open as possible.

DR. AXELROD: I should think it would be perfectly obvious to everyone in this room that the thrust of this program is scientific, that it is Aristotelian logic and not Platonic. That is, we are certainly not going to accept the adversary approach in this review concept. Some of my best friends are lawyers, but this is not their place.

Hopefully, by astute scientific decision-making, we can keep it from the need for legal entrance into the situation. And I do agree with you that in many instances, with everyone being as honest as they can possibly muster, once science enters into the Platonic dialogue, a very fundamental basis disappears. And it's not this Agency it's anyplace, because the Platonic logic is one of adversary approach and winning the argument. Scientists love to win arguments, but it's not the thrust of science. It's examination and prediction on the basis of something. I agree with you.

MR. TOM BLUE: As an extension of an earlier question about criteria for placement on an internal review list, you were mentioning that most of these criteria are essentially external from the Agency. However, can you explain if and how in the mini-economic review or socioeconomic review system where you may decide a product is not a suitable substitute, the criteria in the review process may make a product jump from one list to another?

DR. AXELROD: I would hesitate, as Director of the Criterion and Evaluation Division, to visualize that what impacts on us to make a review are "criteria." The things we just bantered back and forth concerning what leads to an internal review, I wouldn't consider criteria. They are needs, they are pressures, but they are not "criteria."

On the second question, or second part of the first question, Dr. Dale presented one, a very pragmatic and second, a more hypothetical approach to scientific reviews for these alternative chemicals. Contexturally, in those slides were the very basis whereby the proposed hazard for the compound will enunciate a further review. The initial scientific review, the initial mini-review, does not enunciate any proceeding except to go on to in-depth studies.

QUESTION: Let's say you have a hypothetical case, and when the initial scientific review is conducted, you find that you're deficient in data. But the product is not proprietary and it's manufactured by a number of people. With the new section of the law on compensation for data, how will it be handled whereby several manufacturers are going to be involved in this and there's going to be data needed to be generated? Has some thought been given to this?

DR. AXELROD: Yes. That's the basis of a large portion of Dr. Buckley's thrust in the Office of Research and Development. And no more can you get blood out of a stone than information from people who are not making profit. So the need to fill data gaps in a non-proprietary compound would hardly be filled by the industrial sector. And we would turn to either ongoing programs and academia, or internally to either other government agencies which have similar projects on stream or to Dr. Buckley's group in the Office of Research and Development for that type of data development and retrieval.

We want to thank you here at the podium for your indulgence in listening to these review concepts this afternoon, and for, hopefully, digesting them, and for the questions that you've asked. It has given us more food for thought for the development of the program and for other interesting ideas for the future.

PROGRESS IN EPA RESEARCH: NEW DIRECTIONS AND OVERVIEW

John L. Buckley, Ph.D. *

I'd start out by saying that it's nice to be here. I listened all day, and I had the distinct impression that every time a particularly tough problem began to loom, Leonard said something about, "And, you can ask Dr. Buckley tomorrow."

What I did want to speak briefly on is who I am. I don't mean as an individual, but with a title like "Acting Deputy Assistant Administrator for Program Integration," what image does that evoke? It doesn't tell me anything. Therefore, I decided it would be useful to spend a very few minutes speaking on the organization of the Environmental Protection Agency in relation to research, knowing that for many of you here, this is old stuff, but knowing also for some of you, that it's not. So, forgive me, those of you who are eminently knowledgeable about this.

The organization is headed by an Administrator with a Deputy, and there are five Assistant Administrators. One of these five Assistant Administrators is an Assistant Administrator for Research and Development. Under him there are a series of Deputy Assistant Administrators, and I'm acting as one of those. Incidentally, the Assistant Administrator for Research and Development is also acting, since the last one resigned on May 24, 1974.

The other Assistant Administrator of particular interest to us here is the Assistant Administrator for Water and Hazardous Materials, Mr. James Agee. It is in this group that Dr. Korp and my colleagues in the Office of Pesticide Programs work. So, a point to be made, in a sense, is that we work in two different parts of the organization. We both deal with pesticides. But, at the

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*Acting Deputy Assistant Administrator for Program Integration, U.S. Environmental Protection Agency

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time that the Environmental Protection Agency was created, there were bits and pieces that came from quite a number of places.

There were research groups that dealt with pesticides and effects on humans. There was a large program in relation to water pollution. Many of these research groups had similar functions. For example, many of them had health effects research, research on the effects or the fate of substances in the environment, research on analytical methodologies for various compounds and various substrates.

In trying to rationalize the organization in terms of getting the most done for a given number of dollars (which over the period of years, has diminished rather than increased), it seemed to us most useful to organize in terms of health effects, ecological processes, fate and effects, analytical measurement methods, monitoring, and control technology.

We now have in the Office of Research and Development, a Deputy Assistant Administrator for Environmental Sciences, which includes health and that sort of thing; one tor Environmental Engineering; one for Monitoring Systems; and this other one for Program Integration.

After a couple of years, we in Research and Development thought that we knew what we were doing and that what we were doing was pretty good and responsive to the Agency needs. But it turned out that the rest of the Agency neither knew what we were doing, nor felt they had any influence on what it was that we should do. Then the Office of Program Integration was invented to try and serve as a communication link between the rest of the Environmental Protection Agency and the Research and Development group in order that research in this regulatory agency could respond to the real questions and the real problems in the most efficient way — so that we weren't, in the view of the rest of the Agency, "doing our own thing."

We're organized in a headquarters staff relatively small, though often considered excessive. The main function in headquarters is in planning, allocation of resources, and staff support functions.

Our operational research program is carried out through the National Environmental Research Centers (NERC's) and an additional center called the Washington Environmental Research Center. The Washington Environmental Research Center is concerned with socioeconomic research. The other four NERC's are in Corvallis, Oregon, in North Carolina at Research Triangle Park, in Las Vegas, Nevada, and in Cincinnati, Ohio. Each deals with different sets of problems, though these are not exclusively their provinces.

That's probably more than enough, except that I want to emphasize the point that the operational conduct of the research program, once planned and agreed to, is the responsibility of the National Environmental Research Centers, and not of the Headquarters Staff. This is true not only in the intramural work they do in their own laboratories, but also in the expenditure of funds in extramural activities, in both grants and contracts. It's somewhat fuzzy in terms of interagency agreements. Some of these are done from headquarters; others are done in the field.

From the headquarters we do transfer some money, on the order of $4 million a year for the last several years, to the National Center for Toxicological Research, NCTR, in Jefferson, Arkansas. Dr. Cranmer, who will be heading a session tomorrow is the Director of NCTR.

The reason for this particular operation is that long-term, low-dose effects seem to us an important part of our program. How one evaluates these, how one can extrapolate from animal data to man — this whole set of problems dealing with human effects that are less than obvious is the major responsibility of NCTR, and we actively support this in a financial way.

Dr. Cranmer can tell you, if he chooses, the managerial arrangements. Suffice it to say that the Food and Drug Administration is the other contributor, larger in scale than EPA, and they are the managers responsible for the program there, except that the program is substantially influenced by a policy board made up of both agencies.

As far as how much research we do in terms of dollars, the 1975 anticipated budget before the veto that took place a couple of days ago was on the order of $140 million, plus a somewhat larger amount for energy research. Of that $140 million health effects has a little over $35 million. Ecological processes and effects has nearly $40 million. Monitoring systems, which includes analytical quality control and analytical methods development in all media, has about $20 million. Technology development in air and water and solid wastes has a little more than $40 million, and the socioeconomic effects research has about $5 million. Broken out by media and categories, air has about $57 million; water including water supply, just over $45 million; pesticides including alternative chemicals nearly $11 million; with radiation, solid waste, noise, and interdisciplinary research having the balance.

I think that's probably all that I need to say about the mechanics.

I want to come back to the fact that the responsibility of the Office of Research and Development is clear. It is the provision of data and the scientific interpretation of data. It may, at a policy level, also influence decisions in the Agency. That, however, is a separate function and not to be confused with the other.

According to the program, I am to talk about new thrusts in pesticide research.

In looking back there are many things that we know now that we didn't know a decade or a decade and a half ago. There are a lot of things that we know now to look for that we didn't even believe existed then. And there are a lot of these things that are very comforting to us. It's clear, for example, that things don't accumulate indefinitely in anything. If they did, the outcome, of course, would be human beings made up a pure DDT. There's always some kind of a dynamic balance even though there are many details about how such a balance is acquired that we don't know.

But there is a lot about it we do know that we didn't before. What I want to talk about briefly in what was labeled as "new thrusts" is that I believe that one of the most important things that the Federal government can do is to participate in methods development for assessment of pesticidal and other chemicals. Assessment in the sense of predictive in relation to safety — how can we predict better? How do we predict as rapidly as we can and as reliably? What happens to a chemical or what will happen to a chemical in the environment? What kinds of transformations occur? How rapidly do they occur? How can we predict the events that are likely to take place over a long period of time? Over a short period of time?

The question of how you can better make judgments and acquire data that will be useful, is an important one, and that is a kind of a driving force in many parts of our program.

It's true in analytical chemistry. It's true in the use of model ecosystems to evaluate fate of substances. It's true in support of the activity of NCTR, where again we're interested in predicting at an earlier time rather than waiting a human lifetime.

This is one of the areas that we feel very strongly about. Probably we will put more effort into thinking about how you do this with new kinds of pesticide chemicals, the viruses, bacteria, pheromones, and other things of this sort. It isn't that these substances are necessarily all that widespread or important yet, but the fact is that we don't know much about these substances and we're not even sure yet what the right questions are. Therefore we think new methods in that area are important.

You may note that we're not doing much about it yet, but it seems important to me to deal with the non-pesticidal ingredients of pesticidal formulations, those things that all of us in the past have tended to call inert.

We have another program which is called "Alternative Methods of Pest Control," not to be confused with "Alternative Chemicals." The reason it has this name instead of integrated pest control or something of the sort is that we don't want to exclude from it chemical pesticides or other chemicals. We do want to exclude from it some of the routine usages of existing more or less conventional chemicals.

Another thing that we're trying to deal with is understanding of the relationships between biological events noted at high levels of dosage or exposure in relation to "real world" levels. How do you utilize information of that sort or how do you extrapolate it to the levels which are believeable or expectable, even in an extreme case in the environment. I don't have answers but it's one of the driving forces of trying to think about problems of this sort in terms of the real world.

Now if you want to know in any detail about what we're doing, I'm not going to tell you. This room has a fairly large number of people who are recipients or holders of grants and contracts and who are people from our own laboratories. I'm not going to try and list them all because if I do, I will surely miss some. I would encourage you to ask questions of them, particularly in the Friday morning session. If you have any specific questions before that, deal with people who know and not with me, as I am now solely an administrator and communication link between people.

I couldn't overlook the opportunity to make a few gratuitous observations on the basis of sitting here through the day. It seems to me that many of the kinds of questions I have heard, and the implications or connotations of them, could be overcome with an attitude of openess and cooperation. I think I've heard the word "witch hunt" used here. I think there's a certain element of suspicion and I guess I think from my point of view that it's probably unwarranted.

I think that EPA, not only in this program but throughout its other programs, is bound by its Administrator's desires to act in an open fashion. We probably are more open than any other agency. We have taken to heart the Freedom of Information Act. And I can tell you, on those rare occasions when we haven't, the courts have made us wish we had. The point I really want to make is that EPA has behaved and is obligated to behave in an extraordinarily open fashion in making its decisions.

There is another item I'd like to discuss. We've talked about this Alternative Chemicals Program as though it were brand new and in a way it is. On the other hand the same process has been going on long before there was an Environmental Protection Agency. The process consists of the evaluation of a substance and the decision that it will do a certain thing and that the risks associated with it are bearable. The ground rules under which the decisions have been made tend to change with the passage of time, but, nonetheless, the laws have always dealt with both efficacy and safety, and have required consideration of both the risks and the benefits.

It seems to me that what has happened is that now we have been told in a sense by the Congress that we weren't doing as good a job in making these decisions and in weighing the risks and benefits as we ought to have been. We've now formalized a program and to some extent maybe we've compartmentalized it, and we're now describing it in much more explicit terms. We hope it will work better. Nonetheless, it's an extension of a process which has been going on for a very long time.

I would note that it's not substantially different than any other standard-setting process that goes on in EPA, in the sense that you go through a scientific evaluation of what's known and you look at the benefits and the risks, using the best data available and, on the basis of this, you make a social judgment.

Now unfortunately we don't have a world largely populated with Solomons, and from time to time the decisions can certainly be faulted. I think it's important to bear in mind that if we make the decisions openly and if we describe with some precision the basis on which they're made, we can be faulted for not being Solomons but we won't be faulted for being dishonest or stupid. I think that's what this whole process is about.

We all know much more than we did before. We know a lot of questions that are important to ask that we didn't know before. The social climate in which we all live and the attitudes of people are different from what they were in the past. Summing up in a way, I would have said that there was no way that anyone could have predicted some of the events which followed the introduction of DDT. Nobody knew about bioaccumulation of synthetic chemicals. Nobody knew about some of the transformation processes that took place. There were a whole lot of things we learned, and I would submit that the decisions that were made about DDT in the early days to permit it and to use it the way it was used, were absolutely without fault.

I would submit that on the basis of what we know now, one wouldn't have made those same decisions. In a sense, one DDT was inevitable. A second one, in the same sense, is probably inexcusable. We know more. Our understandings are greater. Our sense of values has changed. What's important is that we use the insights that we have and that we draw together the knowledge that we have.

Moreover, we've tended to talk today as though these decisions come out as yes or no decisions, and I suppose finally in a way they do. But never are they really simple yes or no decisions. It's always kind of a muddy shade of gray that you deal with and the man who makes the final decision must select some point at which he makes the decision.

There is also the question of available data. I can't think of a single decision that I know of being made in which all the information one would like to have is available. Yet for an assortment of reasons it's necessary to make decisions.

The last point that I'd like to make is that, in fact, society does accept risks. You know, if you stop and think about it, life itself is very, very risky. But you just have to consider what the alternative is, and to me the alternative is not very satisfactory.

I don't know how informative I've been and maybe I have lectured at you but with that, at any rate, I'd like to close. If there are general kinds of questions or philosophical questions, I would be glad to deal with them today; if they deal with technical questions, I would rather have an assortment of experts answer these the day after tomorrow.

TOWARDS A NEW PERSPECTIVE ON PESTICIDES

Henry J. Korp, L.L.D.*

I feel very encouraged about the sessions we conducted earlier, and as I stated this morning, I feel we have shared a great deal together. While Jim Agee could not be here himself, he asked me to express to you all his appreciation for your participation in this fine effort to understand and support one another.

When we talk about the long-term environmental effects of pesticides, and the potential threat to our resources posed by such effects, I hope we do not imply that this Agency is concerned solely with the problems associated with pesticide use. As I mentioned this morning, we are very interested in the whole environmental situation, in recognizing the attributes as well as the drawbacks to pesticides use. The quality and quantity of our food and fiber, the effectiveness of disease vector control, the sanitation in our homes — pesticides play a vital part in these areas which are important to all of us. The advantages and necessity of pesticides cannot be disputed, and we in EPA are most cognizant of the tremendous role pesticides have played and will continue to play in contributing to man's well being.

But we have learned, too, that the past decade has offered some sobering lessons about the ultimate effects of many products on our supposed prosperity. Certainly, there has been a significant public awakening to the potential of pesticide residues for remaining in the environment, for traveling far from the site of original application, and for accumulating in the food chain. Our society wants, it demands, that the government protect its interest in regulating pesticides so that the benefits of pest control will not be sadly balanced by an ultimate

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environmental tragedy. We thus believe that our past and future responsibility to the public is dual: to ensure that essential pesticide tools are maintained and to ensure that the benefits provided by these tools are not gained at the expense of more valuable resources.

In chatting with many of you today, I have found that some of the basic functions of the Agency which we take for granted should be better explained for the benefit of those who are unfamiliar with the "nitty gritty" of our operations. So, with the indulgence of those of you who are thoroughly familiar with our procedures, I would like to take a few minutes to explain a bit more about the registration process.

As I mentioned this morning, to obtain registration a manufacturer must submit data to EPA to show that (1) the product would be effective for the intended purpose when used as directed and (2) label warnings and cautions when followed are adequate to protect man, livestock, wildlife, and the environment. Data submitted to EPA is carefully evaluated by a staff of scientists to ensure that all the criteria for registration are met. Pharmacologists review a proposed registration to determine that the product will not pose a hazard to health when used as directed and that the warnings on the label will prevent harm when followed. Chemists review the application from the standpoint of the chemical composition and the compatibility of the mixture. Entomologists, weed control specialists, bacteriologists, plant pathologists and physiologists, nematologists, and animal biologists study the application from the standpoint of their particular areas of competence. They determine how effective a pesticide would be against the pests designated on the label, and whether or not the product would cause undesirable side effects on the applicator or environment. No product is registered until our requirements are all fulfilled. How does the consumer know that a product has been registered by this Agency? All registered products must bear an EPA or in the case of older products, a USDA registration number on their labels.

I'd like to briefly point out several of the differences between the old Act and the amended Act which will give you a good idea of what improvements have been made in the regulation process.

First, ALL pesticides will be regulated under the new Act. The old FIFRA required only the registration of products intended for interstate shipment.

Secondly, the new Act provides that pesticides will be classified for either general or restricted use. Under the old FIFRA products were registered or not registered, period. As soon as the general-restricted provision is implemented, those products which we determine may cause an unreasonable adverse effect on the applicator or the environment without additional regulatory restrictions will be classified for restricted use. Those products so designated may be used only by certified applicators or subject to such other restrictions deemed necessary by the Administrator of EPA. Thus, the most potentially harmful pesticides — the ones in the restricted category — may be used only by qualified individuals. We believe this provision will certainly guard against pesticide accidents or improper application.

Thirdly — and this is a very significant change — pesticide misuse is now a violation of the law. Under the old Act, we had no recourse when a registered product was used in variance with label directions and precautions. Now such misuse is subject to civil and criminal penalties.

The final provision which I shall mention is that the Act will afford the public a greater opportunity to participate in the decision-making process of this Agency. We will be publishing notification of applications for registration of all new chemicals or changed use patterns, proposed regulations, and other items which will allow opportunity for public consideration and comment.

The new provisions of the Act are being implemented as regulations. The new sections must be all effective by October 1976.

Many people ask, "What about the food I buy in the market? Am I not subjecting myself and my family to pesticide residues which could be harmful?" Well, EPA is extremely concerned about ensuring that food offered for sale to the consumer will not bear harmful pesticide residues. This Agency thus establishes a tolerance or grants an exemption from a tolerance for all pesticides which are to be used on food or feed crops under the authority designated by the Federal Food, Drug, and Cosmetic Act. A tolerance is the amount of pesticide residue which may remain on or in the treated commodity when marketed. Tolerances are not established by EPA until the pesticide manufacturer submits data to show that (1) the pesticide will not result in residues exceeding the proposed tolerance when used as directed and (2) the proposed tolerance level is safe for human consumption as demonstrated by toxicological tests.

To ensure that residues in foods offered for sale in the marketplace do not exceed the established tolerance, the Food and Drug Administration continually inspects agricultural commodities intended for sale to the public. In addition, the Department of Agriculture inspects meat and poultry for such residues. If any food is found to have residues in excess of the legal tolerance, such food is subject to seizure and destruction. I may also add here that there is a large margin of safety allowed when a tolerance is set; the permissible residue level is actually well below that which would be expected to cause adverse health effects. The consumer may thus be assured that EPA, USDA, and FDA are fully cooperating to protect the public welfare through the strict regulation and enforcement of tolerances.

In speaking of enforcement activities, I must not omit discussing the means by which the Government addresses registration violations. EPA has an Office of Enforcement which determines if marketed pesticide products are conforming to the requirements of the Act. Special inspectors in 10 EPA regional offices collect samples of products throughout the country which are analyzed in EPA laboratories to make certain that the ingredients are true to label claims and that the product is not adulterated with chemicals other than those listed on the label. EPA scientists also make laboratory and field tests on a regular basis to check the effectiveness of registered pesticide products and conduct pharmacological tests to ascertain that safety precautions continue to be adequate.

If a product is found to be in violation of the Act in EPA's tests, appropriate action is taken to ensure that the deficiencies are corrected. In a minor violation, an informal notice to the company concerned may be sufficient. More serious violations may result in a formal notice of violation, seizure of the company's goods, or even prosecution of the violator.

Many people have asked me about EPA's attitude toward new pesticides and pest management techniques. I believe our position can be easily stated: We wish to encourage the development of new pest control methods which are especially intended to increase selectivity and decrease potential harm to the environment or non-target life. You have heard about the research into biological controls — the work involving pheromones (chemical odors which direct many insect activities), juvenile hormones (those hormones which affect the maturing process of an insect), chemosterilants, sterilization by radiation, bacteria controls, virus controls, and cultivation of natural predatory insects. We stand ready to issue experimental use permits for such new activities and have, in fact, already issued one such permit for the hormone insecticide Altosid, which is being tested in 15 states this year. And EPA has made it no secret that we are encouraging work in integrated pest management techniques. We have, in fact, along with the Department of Agriculture and the National Science Foundation, committed over $20 million over the next 3 years to integrated control research.

We would also like to extend our efforts in educating the public about its role in proper pesticide use in the days to come. It may sound simple to say that people should read the label before using a pesticide product. Those who use pesticides in their profession, such as farmers, are usually most careful about strictly adhering to label directions. However, homeowners, who often do not have the proper attitude toward pesticide poisons, are not as meticulous. Unfortunately, many folks will read only far enough to see what a product is supposed to control and then go running about flinging the contents in their gardens and homes. The consumer can do a great deal to protect himself and the environment if he follows four basic steps:

1. Read the directions for use thoroughly. Use only the amount directed at the place and time directed and for the purpose directed. Too many people sadly have the misconception that if one is good, two are better. One car is good, two are wonderful. One tablespoon of concentrate weed killer [illegible] alled for, two will do twice the job. This is a risky misconception and has the potential for destroying the entity one is trying to protect. In short, using a pesticide in variance with label directions is not only illegal, but may also pose a danger to the user, people in the vicinity, other beneficial life, and environmental resources such as air, soil, and water.

2. Read the precautions. Precautions are introduced by one of three signal words — CAUTION, WARNING, or DANGER-POISON. Those in the highest order of toxicity are accompanied by the skull and crossbones. DANGER-POISON denotes those products which are most hazardous, with those in the

WARNING category less potentially harmful, and those in the CAUTION the least hazardous. All pesticides warn the user to KEEP OUT OF REACH OF CHILDREN; in fact, it is best to lock such products out of children's grasp.

3. Observe the ingredient statement and first aid statement, if supplied. These are invaluable if an accident does occur. A copy of the label should always be taken to the physician in such instances.

4. Store the product in a safe place and in the original container. Never, never transfer a pesticide to a soft drink bottle or any other container, especially one attractive to children.

In an effort to find out what can be done to improve labels, EPA contracted with the University of Illinois to conduct a multistudy devoted to finding ways to make the pesticide label a better communication device. As a result of the study, we held the National Labeling Symposium a few months ago to which we invited all registrants to discuss the findings of the Illinois report. We hope our seminar developed many means by which a manufacturer can make his label more readable and attractive to the user. We have also contracted the University of Illinois to conduct another study, this one devoted to investigation of the value of non-verbal symbols (such as faces or traffic signs) on pesticide labels.

Our Office of Public Affairs offers to the public many publications regarding the role of this Agency in pollution control and the role the concerned citizen can play in this vital area. We have just issued a new pamphlet directed to the consumer describing the regulations of pesticides; these pamphlets are available for public distribution.

In closing, I would like to thank you again for your interest in our program and for helping make today a success.

OVERVIEW OF WORLDWIDE PESTICIDE RESEARCH

Morris Cranmer, Ph. D*

Welcome to the second day of this symposium. I believe this day will produce some conversation and insight into the problems before us. My name is Morris Cranmer. I'm Director of the National Center for Toxicological Research. The National Center is in Jefferson, Arkansas. Contrary to some persons' opinions, we do not conduct mega-mouse experiments like in the commercial. I want to thank Dr. Axelrod for making it possible for me to participate in this program. I certainly have had a long-time interest in pesticides research and our laboratory, hopefully, will impact considerably on some of the dilemmas that are facing us in coming to grips with the problems of safety evaluations, especially with respect to environmental chemicals which, of course, include pesticides as a major class.

The National Center for Toxicological Research is a national resource. Its original charter was constructed to be a mechanism by which various Federal agencies could cooperate in problems which impacted especially on their regulatory mission. Currently the Environmental Protection Agency and the Food and Drug Administration are jointly sponsoring the center; however, NCTR, as a national resource, must also be responsive to the university community in providing access to certain research opportunities that might not exist in the parent universities, in stimulating graduate education in toxicology, providing a mechanism for bringing distinguished foreign scientists to the United States to work on special areas of toxicology, and to eventually provide an interface by which the industrial community can work hand in hand with the academic community and the government community in solving some of these problems which are so important not only to our economy, our standard of living, and our health but indeed to the health of the world.

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*Director, National Center for Toxicological Research

Our topic today is "An Overview of Worldwide Pesticides Research. ? What might be included in pesticides research? Certainly pesticides research includes compound development, field tests, safety evaluations, prospective and retrospective evaluations of the sociological, economic, and health impacts, ecological consequences, and marketplace competitivenesses of pesticides.

We are fortunate today to have speakers to discuss each of these topics from the vantage points of the United States government, the academic community, and industry. We are especially fortunate to have several distinguished representatives of the international community to add an absolutely essential perspective to our deliberations. The earth is a closed system and what we in the United States do or do not do impacts extensively on the rest of the world.

Research findings, if correctly translated, are perhaps the commodity most immediately and directly applicable to all parts of the world's family of nations. Research findings, both sociological and economic, and alternate control strategies peculiar to the United States, however, at times can and have been tragically applied to other countries.

The paradoxical pursuit of the pristine purity of absolute safety for synthetic compounds and the near passive acceptance of the consequences of certain naturally occurring compounds is symptomatic of our current inability to deal with the concepts of acceptable risks versus costs and benefits of control strategies. Equally vague are differences in approaches to voluntary versus involuntary risks and exposures.

The attempts to solve a simple equation, including costs, benefit, and risk, will be unsuccessful since the units are not equatable. A more appropriate procedure will be the simultaneous solving of several equations with similar units, with a final social synthesis.

I see in the program that we will continue discussing today and tomorrow, the opportunity to foster the cooperation of all segments of the toxicological community toward improving our regulatory approach to solving our problems.

I would like to draw on two examples, not from the pesticides industry and not from EPA, to avoid an outbreak of napkins being thrown at me, but from equally relevant situations existing in the Food and Drug Administration, a sister regulatory agency to EPA.

Examples that I might offer would include, for instance, cyclamate and DES. If we might explore the cyclamate problem very quickly. Cyclamate was a compound which, from the viewpoint of FDA, was an abused compound; certain components of society used excessive amounts of this material. Certain advertising practices promoted the use of this compound in extraordinarily high quantities. Cyclamate was on the GRAS list, which is a peculiar situation which does not require certain types of toxicological information to be provided as in the registration of a new food additive.

The evaluation of cyclamate produced a toxicological controversy which, in the opinion of the then current Commissioner of FDA, required the removal of cyclamate from the generally accepted as safe list. This does not necessarily mean that it said the compound is toxic. It simply means it can't be generally accepted that it's safe, but indeed a controversy raged over this compound and indeed continues today.

We have here an abuse of the compound. We have a toxicological controversy with inadequate information to completely or unequivocally resolve this controversy. We had a legislative mandate which was inflexible. Here all components of society interacted to produce a situation which resulted in a legal resolution to a problem that, hopefully, science could have impacted on had the information been forthcoming in a timely way.

What was the result on the health of the nation as a result of this decision? There was a considerable shift from the use of cyclamate to saccharine. Now indeed the safety of saccharine is in doubt. The question before us is "Was the public health interest served by concentrating the exposure of our population to a single compound or a few compounds from various compounds that might have been available?" In other words, a suggestion that a consideration of a regulatory impact might have been beneficial. What total risks, in other words, are involved?

Now let us review the DES controversy. Here is a situation which is indeed controversial. We had the Bureau of Drugs, which can apply special risk-benefit type of analysis, approving the day-after pill, which would result in 5 daily 50-milligram treatments with diethylstilbestrol. We had the Bureau of Foods responding to another component of the same law, suggesting that the Commissioner remove the diethystilbestrol approval because of certain residues, two or three parts per billion, of diethylstilbestrol in two or three percent of the livers that were analyzed.

If one does a quick calculation of how much liver you would have to eat in order to equal one day-after pill regime, it comes up to about a million or so pounds of liver. On the surface there seems to be to me a slight discrepancy between the risk and benefits that might be applied through these two parts of the same law.

What could be the side results of this particular decision? As you know, diethylstilbestrol was used to promote the growth of livestock animals. There's some debate as to the efficiency of this growth-promoting process; however, let's say that one-eighth of the soybeans that would be necessary to be consumed would have been saved if diethylstilbestrol was still used.

The Congressional Record contains testimony that says it cost the population of the United States about a half a billion dollars directly because of this decision. Half a billion dollars is roughly the equivalent budget of the National Cancer Institute. I wonder if the benefit from the research of the National Cancer Institute is equal to the risk that was eliminated by the banning of diethylstilbestrol?

However, when we eliminate diethylstilbestrol, we increase the consumption of soybeans internally. That makes less soybeans available for export. When there are fewer soybeans available for export, there are fewer hungry people in other countries that are going to get the soybeans. In addition, shortages adversely affect our balance of payments.

As you know, our balance of payment impacts on the ability to buy expensive foreign oil which is low in sulfur. More oil which is higher in sulfur requires either scrubbers to remove the sulfur or more sulfur dioxide in the air. One might conclude that the people in Los Angeles are going to have more emphysema because of soybeans in the Midwest.

It is an interesting web of involvement that one might begin to develop. How about the diethylstilbestrol situation? Where can we point the blame? The farmers misused the compound. Certain misuses were identified. There's no doubt about that. There were legal arguments that got into the situation as early as 1958 and even before that, which further complicated the situation.

There's no doubt that diethylstilbestrol is a human carcinogen, but it was massive doses of the compound which produced this effect. It is also equally clear that the Bureau of Drugs considered it to be safe for day-after pill treatment under proper supervision. We had only incomplete toxicology provided either by the Federal government or by industry. The controversial dose response studies that were done by Gass are yet to be repeated or explained. The impact of viruses in terms of the development of mammary cancers is yet to be completely explained. There was a regulatory error by the Food and Drug Administration which was reversed by the courts and then, of course, there was the law that we had to respond to which was basically an all or none philosophy. As I see it, each component of society was involved in this particular dilemma; again I think, an example of where we might begin to work together.

In short, all or none, nonscience, no choice, simple solutions, and adversary legal atmospheres are rarely best for society. I might ask whose risk, whose benefit, whose cost? I think the speakers later on this morning will address this. From conversations with them yesterday and last night, I know that a number of the points that they will bring out will be provocative.

Unfortunately, our approach to the accumulation and dissemination of additional data has been no news is good news. Take DDT for example: We have no adequate mechanism for establishing the relative significance of a mouse hepatoma and the exceptionally expansive data base on the safe human use experience.

We must, in my opinion, construct a concert of mutual trust, cooperation, and understanding if we're to speak to these problems, and indeed this symposium is to address mechanisms to approach this problem.

Paramount, I believe, in this process is the promulgation of strategies which encourage and reward the collection of data by all sectors of the community relevant to the protection of health and of the environment. And this strategy must accept that the process of collection of this data will include the discovery of some adverse effects while at the same time providing a better total understanding.

I think that it is completely obvious to everyone in this room that our greatest national contribution is not our jet planes and not our computers and not our ability to get to the moon, but our renewable natural resource, agriculture. When one considers if you added up all the cancer deaths that have ever occurred in the United States from the time there has been a United States, it is less than those deaths which can be attributed to malnutrition and starvation in the world each year. A perspective is definitely needed.

WORLDWIDE PERSPECTIVES OF PESTICIDE RESEARCH

Frederick Coulston, Ph. D. *

Mr. Chairman thank you very much. I'll try to be provocative but I don't feel that way so early in the morning. Our good friend Dr. Axelrod and other people, it's a pleasure to be here. I was given a topic of which I know a little, or should say I know little about it, but we'll try to develop the topic.

I have prepared nothing formal and so we will just have some fun and if you get really provoked, just raise your hand and we'll have a little discussion and that might be more fun than looking at a few slides.

Yesterday I counted the use of the term "benefit-risk ratio relationship" 42 times and then gave up. It was said 42 times and I had the impression that some people knew what it meant and some people didn't know what it meant. I think I'll take just a few minutes before I start and let's play with that phrase a little bit. Then I'll get on to this world prospect topic, but it is part of the total picture.

Risk to what? It's a risk to a hazard and if this is not considered in this context, then you don't have anything but words. If I stand here and tell you I have a compound extremely useful to man, that we must use it, but that it is one of the worst teratogen I have ever seen for rats and mice, what would you do? Would you allow such a compound to be used? But if I also tell you that for dogs and for monkeys and for man, there is no evidence that it had ever been a teratogen, then what would you do? You see this is the concept, the true concept of risk to hazard. How does the animal data predict to man and which species is best.

It's a hazard obviously to mice and rats. The compound I'm talking about

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is aspirin -- common, ordinary aspirin that I'm sure a third of the people in this room took this morning.

I could develop this further but the question of cyclamate came up this morning. I don't want to be on a pesticide program talking about drugs and food additives. That wouldn't be right, but yet this is another perfect example of what I am saying. Cyclamate was never used as cyclamate. In use, it was always mixed with saccharine; so if cyclamate is declared and banned as a carcinogen, the fact is that we never did prove whether cyclamate or the little bit of saccharine caused the problem. The point is, we then switched to saccharine. Now saccharine is accused of producing tumors. What do you do now with saccharine?

In a similar fashion about diethylstilbestrol, just let me add this. The reason that the FDA finally tried to de-list it, was because a substitute was available. I think this is a very important point; that you don't try to ban something useful and needed or restrict its use, unless a very substantial, good substitute for it exists, so that you don't hurt agriculture or the people or the economy. There is a good substitute for DES approved by FDA; these are new non-steroidal estrogenic lactones, which have been very successful in replacing diethylstilbestrol in most cases.

Now to come back to this benefit-risk business. It's a widely overused term. I first heard the term used in 1952 by that grand old man, the father of modern toxicology, Arnold J. Lehman, who was at the Food and Drug Administration at the time. He used to talk to me about this benefit-risk concept. Actually not enough credit is given to the role that the Food and Drug Administration played in those early days when we were shaking off the concepts of pharmacology and biochemistry and betting to grips with the multi-disciplinary approach to the problems of safety evaluation, which included pathology, excretion and distribution of the chemicals, etc. Such great men as Leahman, Fitzhugh, and A. A. Nelson, understood the multidisciplinary approach which developed modern toxicology. They knew that the benefit-risk relationship depended on a good understanding of the hazards involved in terms of the intended use of the chemical. In other words, they knew that the risk must justify the hazard.

Now I'm going to switch to the subject that I'm supposed to be talking about.

In the world today, because of regulatory decisions that have been made, the research in developing new compounds worldwide as pesticides has changed dramatically. When the so called "chlorinated hydrocarbons" were in trouble, such as dieldrin, DDT, the big, major research companies in the world made an obvious decision. They said, we cannot work any longer on substitutes for DDT or on other chlorinated hydrocarbons because even if we found a good one, we'd never get it through a regulatory agency or, the extremists among the environmentalists would hound us to death because of the possibility of build up in the environment, disregarding any good benefit to risk relationship for the intended use of the chemical.

Consequently, there is not, to my knowledge, a major chemical or pharmaceutical company in the world working on true substitutes for DDT or its related compounds. To me this is a tragedy because, as is being learned today in research, these substances are not so persistent in our environment. The work that's being done today in Germany in Professor Korte's laboratory clearly indicates that under the conditions of let's say 50,000 feet up in space, DDT, dieldrin and other compounds, are completely converted to carbon dioxide and water in three weeks, if placed in an environmental situation that mimics the atmosphere. On land it requires about three times as long.

In other words, they have made equipment in which they have exposed the various compounds to ultra-violet light. Photo chemistry is not a new science.

It's been known for a long time, that some chemicals change drastically when exposed to light, air, temperature and humidity. Korte and his colleagues have shown that the rate of change of DDT to carbon dioxide and water is about four percent a week when the DDT is placed on a plate and exposed to ordinary temperature, light, and humidity.

In other words, it would disappear eventually. Now someone very wisely said yesterday that something must happen to DDT because we're not all full of DDT. It is well known that DDT disappears from the surface of the earth and I think now we're beginning to understand some of the reasons why. Under certain conditions, it is possible for DDT to disappear as carbon dioxide and water.

This is research that is in process and was presented in part at the IUPAC meetings in Helsenki. I think many concepts about the bio-degradeability of chlorinated hydrocarbons will be changed. The late Henry Hurtig clearly demonstrated that some of the so called bio-degradeable OP compounds are not so bio-degradeable. Some parts of the molecule persists for long periods of time, sometimes even as long as we thought DDT did. So what is the trade-off here? Now I'll show you a few slides.

What I'm trying to get across to you is that in this whole concept of research, we should not be limited to the carbomates and to the OP compounds. Hopefully somebody someday will make a break-through and find a new type of chemical moiety that would be beneficial and as harmless to man as are DDT and dieldrin.

I've talked to a lot of people recently about the attractants and one of the leaders in this field, recently in Helsenki, told me that to use them alone is hopeless. The attractants will not do the job unless you use an insecticide with them such as DDT. I'm not advocating a return of DDT, please. I agree wholeheartedly with the WHO statement made I think in 1969 at the joint FAO-WHO committee, that DDT should be phased out as soon as an adequate substitute can be found. No one wants to use a chemical that may harm some aspect of the fauna of the world, and from a toxicologist's view point, we don't know what the storage of DDT in our body means. Is it good for us or bad for us? There is no evidence either way. There's no argument about this, but the trade-off is the question -- the benefit-risk is the argument.

Now this leader in the field of attractants said to me, if only we could use a little DDT with the attractants, it would make a great difference. If we could take a plot in the forest, say one mile square, and attract the gypsy moths to the plot and just put the DDT on that plot, then we possibly could achieve our purpose. If you could strategically place these attractants plus the DDT in plots throughout the forest, you might accomplish the control of the insect without spraying the forest completely with DDT. These plots could be observed and studied from all aspects. You can even cover it with a screen to keep the birds out if you want.

In other words, this idea of using conjointly, certain pesticides with attractants or juvenile hormones is a good one and the concept should be pursued.

I was told that he could not get permission to try this concept. He could not get permission to use DDT. Use your own judgment. He and his colleagues should be given the opportunity to try their ideas because I believe it would help solve a difficult problem, threatening our great forests.

So in essence, I've told you about some of the pesticide research going on in the world. There are traps and all kinds of other devices. There are the viruses. There are the bacteria. There's no great hope that these will do a large job. They may be useful in very specific areas but speaking, worldwide, it's hopeless to even conceive of the use of these systems at the present time.

Certainly in a country -- in the developing countries, DDT still will be the pesticide of choice for a long time, provided there hasn't been a development of resistance. If they can for 30 cents, take care of about 30 hectares of land, they are going to use DDT because they have to grow food as economically as possible. If they use DDT, it's going to come right back on us. You've got to realize what you're doing when you say, let's restrict this or ban that. You've got to watch where the winds blow, very literally.

So much then for the worldwide research in the few minutes I have. I wish I could have gone into more detail because it's a problem very dear to my heart. The biggest problem with the OP compounds right now, is the question of demylination, or in general, neurotoxicity. Some of the OP compounds are completely safe when used as directed, others are not. In our institute in Albany, we have a very extensive program just trying to figure out why demylination occurs with certain OP compounds and not with others. This is not federally supported -- it's not government supported. It's a case, where industry on its own has said, we need to solve this problem, help us out. This type of support for research is both desirable and commendable.

What is the problem worldwide? Let's have the first slide.

SLIDE 1

TABLE IV. WORLD PRODUCTION OF ORGANIC CHEMICALS, 1970 [4]

	1950	1970	1985	Release into environment, 1970
Grand total (10^6 t)	7	63	250	20

ORGANIC CHEMICALS – WORLD PRODUCTION

Manufactured	(10^6 t)	Natural sources	(10^6 t)
Solvents	10	Methane	1600
Detergents	1.5		
Pesticides	1	Terpene-type hydrocarbons	170
Gaseous base chemicals	1		
Miscellaneous	7	Lubricating and industrial oils	2-5

This slide (1) shows the worldwide production of chemicals as of 1970. You can see the grand total here in metric tons, ten to the sixth metric tons, and this would represent the amount that probably gets back into the environment. This is a guess, but a very -- very substantial one made by people who know what they're doing. These figures are all sophisticated guesses too, but we have an idea of approximately how much solvents are made, and detergents, and notice that the figure for pesticides represents a very small amount of chemical as compared to the other organic chemicals. Also, on this slide is a very startling figure to me. The terpins hydrocarbons that are formed from trees are greater than the total amount of pesticides used, by many times. This is more of a problem worldwide than worrying about relatively small amounts of pesticides. If I were an EPA research administrator, I'd be putting my money on research aimed at finding out what these terpins do biologically because they are one of our natural problems.

SLIDE 2

TABLE V. ORGANIC CHEMICALS WILL REMAIN THE LEADER
Chemical product classes: Estimates for 1970, 75, 80
made in 1969 [5]

Shipments, 10^9 US dollars (1969)

Key chemical product classes	1970	1975	1980
Chemical and allied products, total	54.4	78.8	114.4
Alkalies and chlorine	0.86	1.25	1.86
Industrial gases	0.71	1.05	1.55
Industrial organic chemicals	8.29	13.26	20.95
Industrial inorganic chemicals	5.13	7.64	11.46
Plastics and resin materials	4.81	7.03	10.41
Synthetic rubber	1.25	1.67	2.29
Man-made fibres	3.76	5.71	8.64

In this second slide, we have tried to project into the future what may happen in 1975 and 1980 to the total production of organic chemicals, based on 1970 figures. These are slides that were prepared for the International Atomic Energy Agency and they're based on extremely good information. Here again, you can see that the industrial organic chemicals are the ones that will continue to increase. The total production of everything in organic and allied chemicals will go up very substantially, all in this decade.

SLIDE 3

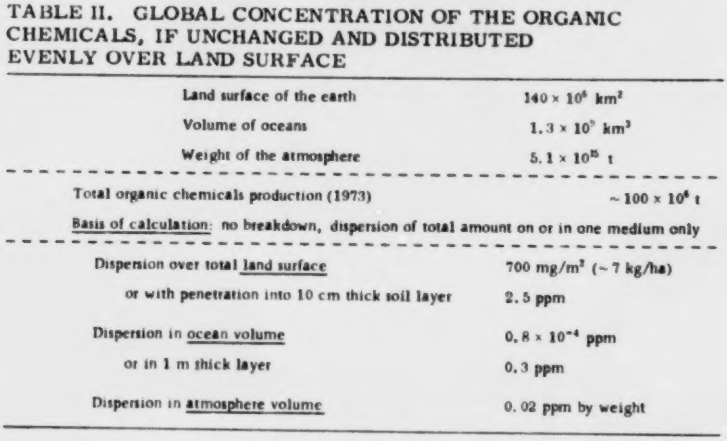


TABLE II. GLOBAL CONCENTRATION OF THE ORGANIC CHEMICALS, IF UNCHANGED AND DISTRIBUTED EVENLY OVER LAND SURFACE

Land surface of the earth	140×10^6 km^2
Volume of oceans	1.3×10^9 km^3
Weight of the atmosphere	5.1×10^{15} t
Total organic chemicals production (1973)	$\sim 100 \times 10^6$ t
Basis of calculation: no breakdown, dispersion of total amount on or in one medium only	
Dispersion over total land surface	700 mg/m^2 ($\sim$ 7 kg/ha)
or with penetration into 10 cm thick soil layer	2.5 ppm
Dispersion in ocean volume	0.8×10^{-4} ppm
or in 1 m thick layer	0.3 ppm
Dispersion in atmosphere volume	0.02 ppm by weight

Slide 3. Here is the slide that I think is the most fun because it tells you a great deal and gives you a chance to speculate. The total land surface of the earth as shown in this figure is 140 times ten to the sixth square kilometers. These are synthetics; organic chemical production, 1973, and no breakdown, no dispersion of total amounts or anything else. This is just calculating what would

happen if you just took the total production and spread it out on the earth. It comes out to 2.5 parts per million,: if you have a ten centimeter, fixed soil layer.

Now I'm supposed to talk about world problems, so here is some of the problem. In the ocean volume, a one meter thick layer, it will come out to .3 parts per million, and dispersion in the atmospheric air, .02 parts per million.

SLIDE 4

TABLE III. GLOBAL CONTAMINATION FROM PESTICIDES, NITROGEN FERTILIZERS AND, FOR COMPARISON, ORGANIC CHEMICALS

Land surface of the earth	14×10^9 ha
Agriculture (a)	1.4×10^9 ha
Pastures (p)	3×10^9 ha
Forests (f)	4×10^9 ha

Input to soil per year (no conversion, no evaporation or leaching)

	World production (10^6 t/yr)	kg/ha in area of use		When distributed over total land surface	
		locally	globally	(kg/ha)	(mg/m^2)
Pesticides	1	2-4	0.12 (a/p/f)	0.07	7
Nitrogen fertilizers	15	70	3.4 (a/p)	1.1	110
Total organic chemicals	100		1.80 (a/p/f)	7.0	700

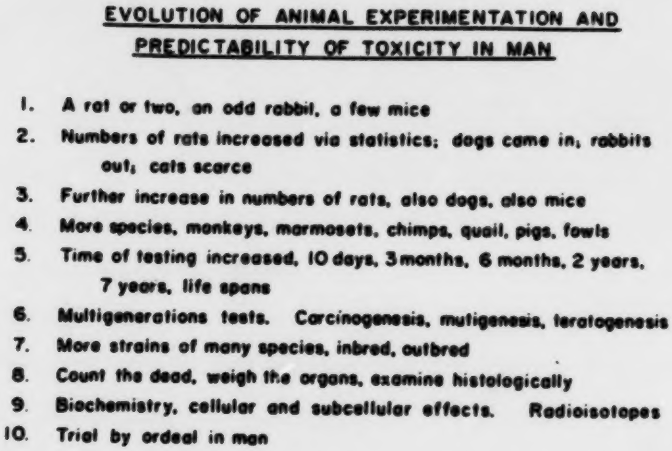
Slide 4. I Just want to give you some idea of what we're talking about. These are the problems. Now, if you take pesticides as used today and talk about global contamination from pesticides, you come up with this figure. If you assume a land surface of agricultural lands, pastures, forests as these figures here do in hectares, and if you also consider that no conversion of the chemicals happened, then you find if you come down to this part of the slide that the world production of organic chemical 100 x 10^6 metric tons a year in total

and 1 x 10^6 is pesticides, and 15 x 10^6 nitrogen fertilizer. Now these are figures that are kind of fun.

If you go to this column, you will see that when pesticides are distributed over the total land surface, you come up with a figure of seven milligrams per square meter of land surface, or, putting it the other way, .07 kilograms per hectare. Nitrogen fertilizers are much more, while the total organic chemicals produced are, in general, almost another order of magnitude.

So the pesticide problem is not really so great as compared to the total amount of chemicals that we are actually putting on the earth each year. In my opinion., with the research that's being done now in many laboratories, the pesticide safety problem of residues can be very soon explained on the basis of biodegradeability. And remember, these figures are presented with no conversion, no evaporation, no leaching, so that we're talking about the best total figures of use that can be put together.

SLIDE 5



EVOLUTION OF ANIMAL EXPERIMENTATION AND PREDICTABILITY OF TOXICITY IN MAN

1. A rat or two, an odd rabbit, a few mice
2. Numbers of rats increased via statistics; dogs come in, rabbits out; cats scarce
3. Further increase in numbers of rats, also dogs, also mice
4. More species, monkeys, marmosets, chimps, quail, pigs, fowls
5. Time of testing increased, 10 days, 3 months, 6 months, 2 years, 7 years, life spans
6. Multigenerations tests. Carcinogenesis, mutigenesis, teratogenesis
7. More strains of many species, inbred, outbred
8. Count the dead, weigh the organs, examine histologically
9. Biochemistry, cellular and subcellular effects. Radioisotopes
10. Trial by ordeal in man

Slide 5. Having briefly defined what the world problem is -- having talked a little bit about benefit-risk, let me just review with you very briefly what decision-making has to do with the benefit-risk ratio. This is a history of toxicology. It begins in 1940.

In 1940, it was possible to get a drug or a food additive cleared at the Food and Drug Administration in Washington, D. C., just by studying the chemical in a few rats, a few rabbits, an occasional dog, with a little pharmacology. A 30 day experiment in rats was sufficient and you got clearance as to safety of the chemical. Not efficacy. I'm only talking about safety evaluation here.

Then we soon learned, beginning in World War II, in the 1940 - 1946 period, that this wasn't sufficient. So, we began to increase the numbers of animals. We used statistics, we used more dogs. We couldn't even get a cat in Chicago, where I worked. They were all being used up by research laboratories of one sort or another. We increased the numbers of animals, because of the lack of our assurance of safety. We began to use all kinds of species; as early as 1935 -- I was using rhesus monkeys for these kind of toxicity studies and, during the war, they were used extensively. Now we have the chimps and other non-human primates.

Then the uncertainty of these procedures led to this marvelous extrapolation that if two years isn't enough to decide whether it's safe, let's make it seven years, let's make it ten years; so we kept increasing the number of years and now you finally have life span studies of animals. You do multi-generation studies and carcinogenicity, mutagenic, teratogenic experiments. We use strains of strains and strains of species. We in-bred them: we out-bred them. We count the dead ones and we weigh the organs and we examine them. We do histro-chemistry and electron microscopy and bio-chemistry. Now we're in the insides of the cells, studying the sub-cellular organelles. But, in the final analysis, you've got to go to man, because we just don't know how to predict completely from animal data to human response. We're learning.

SLIDE 6

PREDICTABILITY SCORE OF DRUG REACTIONS FROM ANIMAL STUDIES

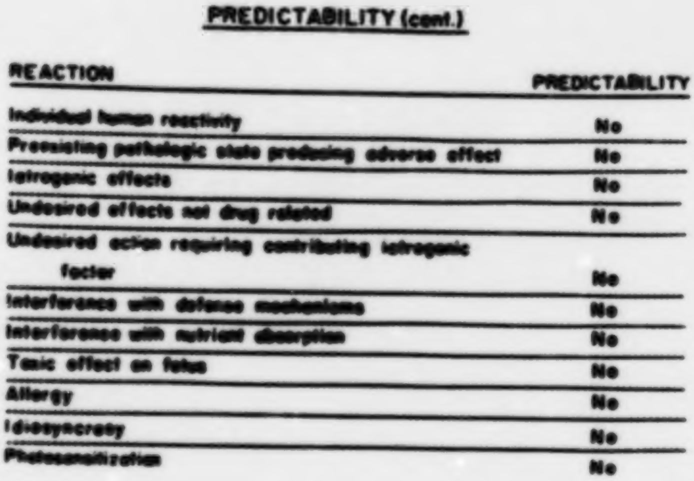
REACTION	PREDICTABILITY
Direct toxicity to an organ system	Yes
Safety factor	Limited
Intended drug action	Yes
Undesirable (wrong organ, biochemical damage)	Yes, through use of large doses
Hemolytic reaction.	Usually
Drug or metabolite storage	Yes

The next slide (6) shows you the kind of things we can predict and this is very important in considering your benefit-risk ratios.

Ordinarily you don't go to man to find out if the animal tests were right or not. In many cases, we do go to limited studies in man even with pesticides and food additives to make sure of the safety evaluation based on animal studies. Remember my good friends, you put 220 million people at risk based on animal data. This would never happen with a drug, of course, because you do some human trials. Your information as to predictability must be even better than with drugs, and unfortunately, it often isn't. So what do you do? That's your dilemma. We try to figure out something to do; but we'll help.

The point is, we have a very good record in predicting these sorts of toxic effects; direct toxicity to an organ system, safety factors, intended drug use, undesirable long range organ effects, which is quite common in carcinogenesis studies, hemolytic reactions and then the metabolite storate, and so on.

SLIDE 7



PREDICTABILITY (cont.)

REACTION	PREDICTABILITY
Individual human reactivity	No
Preexisting pathologic state producing adverse effect	No
Iatrogenic effects	No
Undesired effects not drug related	No
Undesired action requiring contributing iatrogenic factor	No
Interference with defense mechanisms	No
Interference with nutrient absorption	No
Toxic effect on fetus	No
Allergy	No
Idiosyncrasy	No
Photosensitization	No

Slide 7. But where we are almost completely lost is in all of these things I've listed; individual human reactivity. Remember this is predictability from animals to man and here's where we can go wrong. We don't know anything about pre-existing pathologic states producing adverse effects. We don't use sick animals in our animal studies. We have very few real models of disease anyway, in most instances, except in the parasitic type infections and micro-biological infections, in general. We don't have a good model for high blood pressure and

how do you know the pesticide isn't going to affect high blood pressure. You see, we don't have a good model so the toxicologists have to worry about this a little bit. Eventually the pharmacologists, I'm sure, will help us out. The key thing down here is toxic effect on the fetus.

We have no certain way yet to predict teratology from animal to man. We're hopeful that the monkey model helps a little more than most studies. I remind you that thalidomide never affected the rat or the mouse, completely worthless, and if we had stipulated the use of rodents in guidelines, we would have missed the danger of thalidomide anyway. Be very careful with your guidelines is all I'm saying. In fact, if I give you any advice this morning, do not make guidelines that are too detailed and restrictive.

Every one of those companies that is sending you material, have experts who know what tests to do; then you can judge whether he did it right or not. You don't have to have guidelines that are so restrictive they stop the development of scientific thinking. I often go abroad and I find in some countries that they are using guidelines that the FDA put out in 1954 that are wrong by today's thoughts. Guidelines should change almost every day, anyway.

If I tell you now there is no test for mutagenesis acceptable to everyone, to most scientists that I know of, including those at the FDA, how are you going to establish guidelines then for mutagenesis, except to say, please fellows, do something. Let us see what you do. Maybe they'll develop a new test.

What's the guideline for teratogenesis? Are you going to ask for three generation, four generation? I don't know. As far as specific guidelines for carcinogenesis, forget it. Last week in Saratoga -- and there are at least four people in this room who heard the discussions -- some of the most eminent pathologists and cancer research men in the United States said, throw the mouse test out. It's essentially worthless in predicting carcinogenesis to man. If you want the names of the people that made this statement, I'd be delighted to give them to you later; but their remarks will be published, anyway.

Now I'm not suggesting to throw the mouse test out. I'm trying to say, understand the mouse, but don't base decisions on whether a chemical produces a hepatoma only in a mouse, but rather on the fact that it does or does not in a rat and in a dog and in a monkey and in man. If the hepatoma only occurs in the mouse, you've got a problem.

The whole problem with the carcinogenesis of chlorinated hydrocarbons in mice literally depends on the differences between strains of mice. In some there may be established a no effect level and a dose response relationship. In 1969, some in the audience will remember that the WHO-FAO group on pesticide residue made a statement that we could have a no effect level and a dose response curve to a teratogen.

Many members of that group agreed that this statement could also apply to a carcinogen. One man objected strenuously, and by the way, that one man now has changed his mind and he agrees with what I am saying. We did say, however, in '69, that more research must be done to establish whether a no effect level can exist for a carcinogen and whether a dose response curve is possible. The answer is that with DDT, with phenobarbital, with dieldrin, with mirex, this is so. If I could just leave this message with you, I'll be happy. If you take a low level of a compound which may only cause a hepatic-parenchymal cell to hypertrophy -- to get bigger — you exercise a muscle, it gets bigger, drink a lot of salt or a lot of water, your glomerular cells get bigger, you eat a lot of fat and your hepatic cells get bigger. In other words, this is a normal, physiologic process of how the body handles a chemical and metabolizes it, passes it on in a form that it can be excreted. But if you keep pumping into the liver day after day, a large amount of chemical then the cell cannot handle it and the cell gets bigger -- and the cell gets bigger -- and the hepatic liver cell may now be two to three times its normal size, and you keep pumping the chemical in, what do you expect? The cell will die.

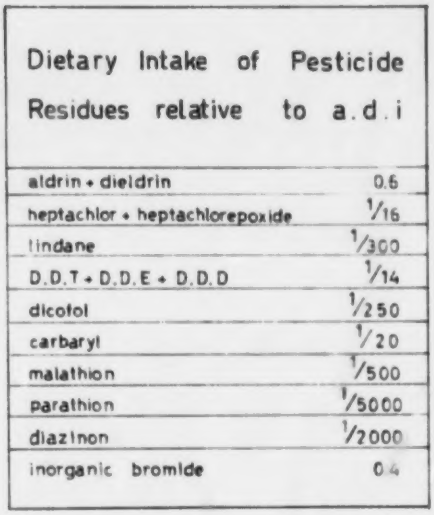
Now either the cell is replaced by another normal hepatic cell or it may be replaced by an abnormal one and hyperplasia may occur. When you get hyperplasia, you can get hepatic nodule formation, and you can get true carcinomas, but why shouldn't you expect this? What darn fool would keep pumping chemicals to the cell at high levels that the cell cannot handle. If I had a big balloon and I blow air in it and I fill it to its normal size and then I blow it twice the size and then I try to blow it four times the size, it will burst, and that's exactly what you're doing when you're pumping in these chemicals during these long term, life-time studies, keeping the dose constant at high levels. You say, oh eureka, I found a tumor. Why shouldn't you find one?

I heard a prominent controversial FDA scientist on television this morning. She has just written a book stating that many common food additives should be banned. She said there are many people who believe one molecule will cause a cancer. Well this may be true. A few molecules could cause a cancer, if it's a primary carcinogen, but the chlorinated hydrocarbons we're talking about, DDT, dieldrin, and phenobarbitol, are not primary carcinogens. At low level dosages, a no effect level can be established; nothing happens in the animals, even in highly susceptible mice, that's the point; a no effect level and a dose response relationship can be established.

Now if I had to consider a nitrogen mustard, it could very well be that 100 molecules could cause cancer because these are highly potent carcinogens. You must recognize you don't throw everything in the same pot and say, oh I got a tumor, therefore it's cancer. This is not the correct way to look at it. You must separate in your thinking those chemicals that change cell structure and identities from those that mechanically are stored in excess in cells.

I'm going to go very fast on the slides because I'll try to finish in two minutes.

SLIDE 8



Dietary Intake of Pesticide Residues relative to a.d.i

aldrin + dieldrin	0.6
heptachlor + heptachlorepoxide	1/16
lindane	1/300
D.D.T + D.D.E + D.D.D	1/14
dicofol	1/250
carbaryl	1/20
malathion	1/500
parathion	1/5000
diazinon	1/2000
inorganic bromide	0.4

Duggan, Lipscomb 1969

This slide (8) presents a very important point I want to make. This is an old slide of our good friend, Dr. Dugan. Many people object to these kind of calculations based on the ADI and the amount of chemical that's found in the bread basket. But somebody talked about it yesterday and I thought there was a point to be made; here is such a slide.

As far as I know, the ADIs of any pesticide in food has never been exceeded except for one year I think somewhere around this time (1969) or a year after, when the residue of dieldrin equalled the ADI in the market basket survey, but to my knowledge, it never has been exceeded. Now, if this is true, why are we

2

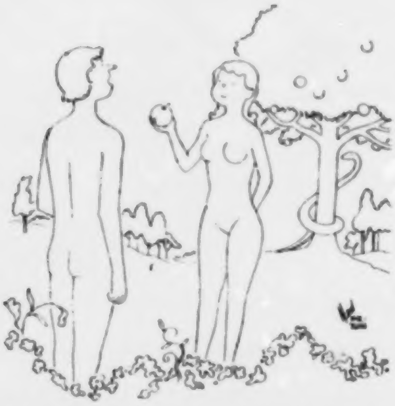
paying all this attention to safety -- why are we so concerned about a lot of these pesticides that are being used properly for their intended use in agriculture? If they're being used properly, then this is the outcome, our food is safe. If our food is safe, then maybe we're spending too much of our effort and time worrying about some of the things we heard about yesterday. Maybe we have reached the point of thinking that safety depends on a safety overkill with hundreds of times safety factors; safety factors for what - mice or men!

As far as the public is concerned, men like Dr. Lu (WHO) and Dr. Turtle (FAO) and the people of the FDA have their jobs. We mustn't forget that over the years they protected all of us. This is all I'm trying to say. To my knowledge, we have never exceeded ADIs for pesticides in the bread basket studies done in the USA.

Question: Are those average figures or maximum?

Mr. Coulston: No, these are average I'm sure, but it doesn't matter. Go on to the last slide. (9). Now here -- here's an example of the whole benefit-risk relationship.

SLIDE 9



"I certainly will not take a bite. How do I know it isn't full of chlorinated hydrocarbons, benzene hexachloride, or organic phosphates."

This is Adam and Eve in the early days of mankind. Now Eve offers Adam an apple. Now he must decide the benefit risk relationship. What would have happened to the human race if he had answered as in the caption, "I certainly will not take a bite of the apple. How do I know it isn't full of chlorinated hydrocarbon, benzine, hexachloride, organic phosphates, tec." I think this kind of sums it all up. Thank you very much.

DR. COMMONER: I'd like to make a few comments on a number of specific points that have been made by Dr. Coulston and then make some general comments.

First, let's take the slide that dealt with the daily intake of various pesticides and as I recall, the highest value relative to the acceptable level was 0.6. I asked Dr. Coulston whether that value was an average and apparently it is. What does that mean? That means that among a large population in which the average is six-tenths of the acceptable daily intake, there must be some proportion of people who are getting more and some who are getting less. In other words, that average does not really inform us adequately about the risks confronted by individuals in the population.

What we need to know is the frequency distribution curve. If that curve is anything like the corresponding ones for other environmental agents, it will have a log-normal form, tailing off to the high side. As a result, a significant proportion of the population would be getting more than the acceptable daily intake. On another point, I think that it is scientifically unacceptable to judge the environmental impact of any material by dividing the amount disseminated in the entire planet by the surface of the earth. For example, one slide showed that the world average depositinn of nitrogen fertilizer is 1.1 kilos per hectare, yet in the state of Illinois, the rate of application is 100 times higher than that.

Exposures to nitrate levels in surface waters derive from that actual deposition rate and not from the world average.

DR. COULSTON: Sir, I didn't invent it. I told you where the slide came from. It came from the International Atomic Energy Agency. Anyway, the slide is ten to the sixth metric tons.

DR. COMMONER: Now let me comment on the question of carcinogenesis. Take, for example, a problem that troubles many people, -- that a carcinogen is often active in one test species and not in another; that mice, for example, tend to be more responsive to carcinogens than rats.

We now understand the reason for the differential response of test species to carcinogens. The key observation is that what we call the carcinogen is almost always not the active material. Rather, it is first metabolized, very often but not necessarily in the liver, to yield the active material. For example, one of the most potent carcinogens, AAF, is a very active carcinogen in the rat, but is inactive in the guinea pig.

However, it was discovered that N-hydroxy AAF is produced in the liver of AAF-fed rats and that is the active carcinogen. When this AAF metabolite was injected into a guinea pig, tumors were produced. What does this mean about the carcinogenic hazard to man?

We need to ask: To what degree do the bio-chemical properties of the human liver resemble that of the guinea pig or the rat, and what variation in these properties occurs among different individuals? There is now evidence that the enzyme system that acts on carcinogens is genetically determined in man so that there are genetic differences among people, which may very well explain the differential response of people let's say to smoking.

The reason why mice are so sensitive to carcinogens is that the strains of laboratory mice have a much wider genetic variability than rats. Strains of mice can be selected that are extraordinarily sensitive to carcinogens simply for the reason that we have a wider spread of genetic variation in the available animals.

I only want to make one final comment. I've been very impressed in this meeting with the opportunity for the people in the commercial field to come in contact with the thinking not only of EPA personnel, but also of people in the academic world. It's clear that the decisions are going to have to be made in the commercial world.

I should like to suggest that the industry will be misled about the nature of pesticide problems unless the points such as those I have just discussed are carefully considered.

DR. COULSTON: Dr. Commoner, let me just say this. I don't disagree with anything you say. This has been going on for 20 years. We who are in this field of toxicology have considered everything you've said and we think we understand toxicology. I'll say this then, I'm being very conciliatory, I don't think you listened to all my points with an open mind, but that's all right. Arnold Lehman (the grand old man of toxicology) used to say, you too can be a toxicologist in two easy lessons, each ten years long.

THE ROLE OF THE WORLD HEALTH ORGANIZATION IN PESTICIDE RESEARCH

Frank C. Lu, M. D.*

WHO's role in pesticide research falls into two distinct areas: One concerns public health uses and the other, agricultural uses.

Some human diseases are transmitted by insects and other vectors. Examples of important diseases of this type are malaria and schistosomiasis, which affect millions of people in the world. One useful measure to control such diseases is to reduce the relevant vectors by the use of pesticides. WHO, in collaboration with research scientists in industry, governments, and universities, has tested many potential pesticide chemicals. The relative values of these chemicals are assessed with respect to their effectiveness against the vector, their toxicities in laboratory animals, and their health hazards to the users and the exposed population.

WHO's activities in the other area need a bit more elaboration because they are not directly concerned with research, but they contribute, nevertheless, significantly in an indirect way.

First of all, I would like to point out that WHO's objective is the attainment by all peoples of the highest level of health. In order to achieve this objective, WHO has a number of functions, one of which is the elaboration and promotion of food standards. Because at an international level the supply of food is also a matter within the competence of FAO, the two international agencies have established a Joint Food Standards Programme. The principal organ of the Programme is the Codex Alimentarius Commission. At present, the membership of the Commission consists of 106 member states of WHO and/or FAO.

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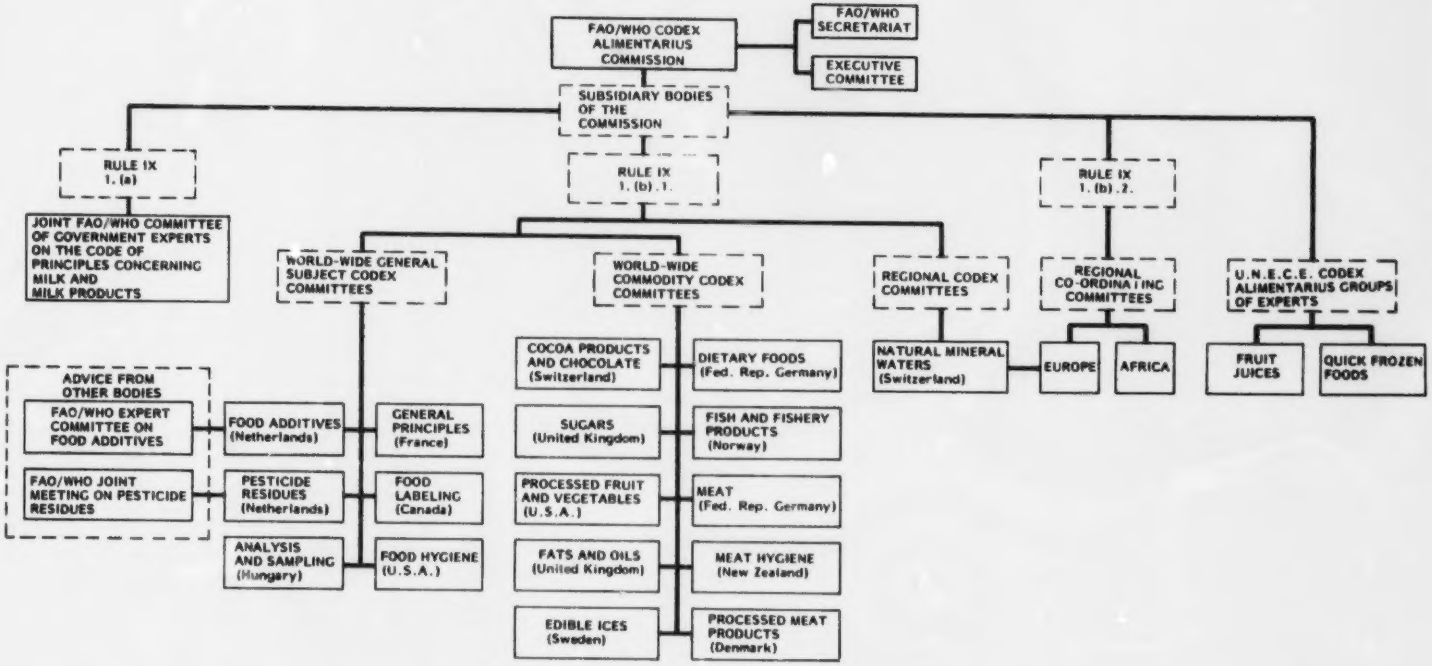
*Chief, Food Additives, World Health Organization

The Commission is assisted by the Joint FAO and WHO Secretariat and 20 subsidiary bodies in carrying out its wide-ranging activities. The activities are best shown by the organizational chart of the Commission (Figure 1). The subsidiary bodies, also known as Codex Committees, fall into two main categories: One deals with general subjects such as food additives, pesticide residues, food hygiene, and methods of analysis and sampling; the other deals with groups of specific food commodities. As the Commission has to deal with many subjects, it has established criteria to determine the priorities. The criteria for general subjects and commodity standards are listed in Figures 2 and 3 respectively. In both cases the protection of the health of the consumer is the prime criterion.

A commodity standard contains the following provisions: scope, description, essential composition and quality factors, food additives, contaminants, hygiene, weights and measures, labeling, and methods of analysis and sampling. Limits for pesticide residues are not included in the commodity standards but constitute separate standards.

The procedure for the elaboration of Codex standards is as follows: The Commission decides that a standard should be elaborated and sets up a Codex Committee or entrusts the elaboration to some other body. The Codex Committee or other body produces a draft, which at this stage is a "proposed draft standard." It is circulated to governments for comments and may be considered and further amended by the appropriate coordinating committee in the case of a regional or group of countries proposal. Otherwise, the "proposed draft standard" will be considered or further amended by the Codex Committee or other body. It is then presented to the Commission as a "proposed draft standard" and the Commission uses it as the basis for producing a "draft standard." This is sent to governments for comments, and in the light of these comments and after further consideration by the Coordinating Committee or Codex Committee or other body, the

Figure 1


FAO/WHO CODEX ALIMENTARIUS COMMISSION
FAO/WHO SECRETARIAT
EXECUTIVE COMMITTEE
SUBSIDIARY BODIES OF THE COMMISSION
RULE IX 1. (a)
RULE IX 1. (b).1.
RULE IX 1. (b).2.
JOINT FAO/WHO COMMITTEE OF GOVERNMENT EXPERTS ON THE CODE OF PRINCIPLES CONCERNING MILK AND MILK PRODUCTS
WORLD-WIDE GENERAL SUBJECT CODEX COMMITTEES
WORLD-WIDE COMMODITY CODEX COMMITTEES
REGIONAL CODEX COMMITTEES
REGIONAL CO-ORDINATING COMMITTEES
U.N.E.C.E. CODEX ALIMENTARIUS GROUPS OF EXPERTS
ADVICE FROM OTHER BODIES
FAO/WHO EXPERT COMMITTEE ON FOOD ADDITIVES
FAO/WHO JOINT MEETING ON PESTICIDE RESIDUES
FOOD ADDITIVES (Netherlands)
PESTICIDE RESIDUES (Netherlands)
ANALYSIS AND SAMPLING (Hungary)
GENERAL PRINCIPLES (France)
FOOD LABELING (Canada)
FOOD HYGIENE (U.S.A.)
COCOA PRODUCTS AND CHOCOLATE (Switzerland)
SUGARS (United Kingdom)
PROCESSED FRUIT AND VEGETABLES (U.S.A.)
FATS AND OILS (United Kingdom)
EDIBLE ICES (Sweden)
DIETARY FOODS (Fed. Rep. Germany)
FISH AND FISHERY PRODUCTS (Norway)
MEAT (Fed. Rep. Germany)
MEAT HYGIENE (New Zealand)
PROCESSED MEAT PRODUCTS (Denmark)
NATURAL MINERAL WATERS (Switzerland)
EUROPE
AFRICA
FRUIT JUICES
QUICK FROZEN FOODS

JOINT FAO/WHO FOOD STANDARDS PROGRAMME

Figure 2

Criteria Applicable to General Subjects

Consumer protection from the point of view of health and fradulent practices.

Diversification of national legislations and apparent resultant impediments to international trade.

Scope of work and establishment of priorities between the various sections of the work.

Work already undertaken by other international organizations in this field.

Type of subsidiary body envisaged to undertake the work.

Figure 3

Criteria Applicable to Commodities

Consumer protection from the point of view of health and fradulent practices.

Volume of production and consumption in individual countries and volume and pattern of trade between countries.

Diversification of national legislations and apparent resultant impediments to international trade.

Amenability of the commodity to standardization.

Number of commodities which would need separate standards indicating whether raw, semi-processed, or processed.

Work already undertaken by other international organizations in this field.

The type of subsidiary body envisaged to undertake the work.

Commission reconsiders the draft and adopts it as a "recommended standard." This is sent to governments for acceptance and is published in the Codex Alimentarius as a Codex standard, when the Commission determines that it is appropriate to do so in the light of the acceptances received.

Following this elaborate procedure the Commission, with the assistance of its subsidiary bodies, has already adopted a number of Codex standards (Figure 4) that have been translated, printed, and transmitted to the governments of member states for their consideration for acceptance. In addition, the Commission has elaborated a number of methods of analysis and codes of practice. These are listed respectively in Figures 5 and 6. Additional standards, methods, and codes have been adopted by the Commission, but these are being translated and/or printed before submission to the governments.

Figure 4

List of Recommended CODEX Standards Issued To-Date to Governments for Acceptance, February 1974

Labeling

CAC/RS	1-1969	-General Standard for the Labeling of Pre-packaged Foods

Pesticide Residues

CAC/RS	2-1969	-Tolerances for P. R. - 1st Series
CAC/RS	35-1970	-Tolerances for P. R. - 2nd Series
CAC/RS	43-1971	-Tolerances for P. R. - 3rd Series

Fish

CAC/RS	3-1969	-Canned Pacific Salmon
CAC/RS	36-1970	-Quick Frozen Gutted Pacific Salmon
CAC/RS	37-1970	-Canned Shrimps or Prawns
CAC/RS	50-1971	-Quick Frozen Fillets of Cod & Haddock
CAC/RS	51-1971	-Quick Frozen Fillets of Ocean Perch

Figure 4 (continued)

Sugars

CAC/RS	4-1969	-White Sugar
CAC/RS	5-1969	-Powdered Sugar (Icing Sugar)
CAC/RS	6-1969	-Soft Sugars
CAC/RS	7-1969	-Dextrose Anhydrous
CAC/RS	8-1969	-Dextrose Monohydrate
CAC/RS	9-1969	-Glucose Syrup
CAC/RS	10-1969	-Dried Glucose Syrup
CAC/RS	11-1969	-Lactose
CAC/RS	12-1969	-Honey (European Regional Standard)
CAC/RS	54-1971	-Powdered Dextrose (Icing Dextrose)

Processed Fruits and Vegetables

CAC/RS	13-1969	-Canned Tomatoes
CAC/RS	14-1969	-Canned Peaches
CAC/RS	15-1969	-Canned Grapefruit
CAC/RS	16-1969	-Canned Green Beans & Wax Beans
CAC/RS	17-1969	-Canned Applesauce
CAC/RS	18-1969	-Canned Sweet Corn
CAC/RS	42-1970	-Canned Pineapple

Edible Fats and Oils

CAC/RS	19-1969	-General Standard for Fats & Oils not Covered by Individual Standards
CAC/RS	20-1969	-Edible Soya Bean Oil
CAC/RS	21-1969	-Edible Arachis Oil
CAC/RS	22-1969	-Edible Cottonseed Oil
CAC/RS	23-1969	-Edible Sunflower Seed Oil
CAC/RS	24-1969	-Edible Rape Seed Oil
CAC/RS	25-1969	-Edible Maize Oil
CAC/RS	26-1969	-Edible Sesame Seed Oil
CAC/RS	27-1969	-Edible Safflower Seed Oil
CAC/RS	28-1969	-Lard
CAC/RS	29-1969	-Rendered Pork Fat
CAC/RS	30-1969	-Premier Jus
CAC/RS	31-1969	-Edible Tallow
CAC/RS	32-1969	-Margarine
CAC/RS	33-1970	-Olive Oils
CAC/RS	34-1970	-Mustard Seed Oil

Figure 4 (continued)

Edible Fungi

CAC/RS	38-1970	-General Standard for Fungi and Fungus Products
CAC/RS	39-1970	-Edible Dried Fungi
CAC/RS	40-1970	-Fresh Fungus "Chanterelle" (European Regional Standard)

Quick Frozen Fruits and Vegetables

CAC/RS	41-1970	-Quick Frozen Peas
CAC/RS	52-1971	-Quick Frozen Strawberries

Fruit Juices

CAC/RS	44-1971	-Apricot, Peach and Pear Nectars
CAC/RS	45-1971	-Orange Juice
CAC/RS	46-1971	-Grapefruit Juice
CAC/RS	47-1971	-Lemon Juice
CAC/RS	48-1971	-Apple Juice
CAC/RS	49-1971	-Tomato Juice
CAC/RS	63-1972	-Concentrated Apple Juice
CAC/RS	64-1972	-Contrated Orange Juice

Foods for Special Dietary Uses

CAC/RS	53-1971	-Foods with Low Sodium Content (Including Salt Substitutes)

Figure 5

List of Recommended International Codes of Practice, February 1974

CAC/RCP	1-1969	-General Principles of Food Hygiene
CAC/RCP	2-1969	-Canned Fruit and Vegetable Products
CAC/RCP	3-1969	-Dried Fruits
CAC/RCP	4/5-1971	-Dessicated Coconut and Dehydrated Fruits and Vegetables Including Edible Fungi
CAC/RCP	6-1972	-Tree Nuts

Figure 6

List of Related Recommended Texts Sent to Governments, February 1974

CAC/RM	1/8-1969	-Methods of Analysis for Sugars
CAC/RM	9/14-1969	-Methods of Analysis for Fats and Oils
CAC/RM	36-39-1970	-Methods of Analysis for Processed Fruits and Vegetables
CAC/RM	32-1970	-Standard Procedure for Thawing of Quick Frozen Fruits and Vegetables
CAC/RM	33-1970	-Standard Procedure for Cooking of Quick Frozen Vegetables
CAC/RM	42-1969	-Sampling Plans for Prepackaged Foods (AQL 6.5)

WHO and FAO have been convening joint meetings on pesticide residues since 1961. The current series of Annual Joint Meetings of the FAO Working Party and the WHO Expert Committee on Pesticide Residues began in 1966. The agenda of the Joint Meeting is usually drawn up on the basis of the recommendations of the Codex Committee on Pesticide Residues, which is attended not only by delegates of governments but also by representatives of industrial concerns and of international organizations. Once the list is drawn up, it is sent to the manufacturers of pesticides to solicit published and unpublished data. Attempts are also made to search the open literature. The information so collected is reviewed and summarized by temporary advisers to WHO; their working papers are sent to the manufacturers who submitted the data. The manufacturers are, in general, extremely cooperative in reviewing the working papers and in making comments which are given full consideration by the Expert Committee at its meeting. On the basis of the original data and the temporary advisers' papers, a second set of working papers is prepared by the members of the Expert Committee. All these papers are circulated to the members before the meeting.

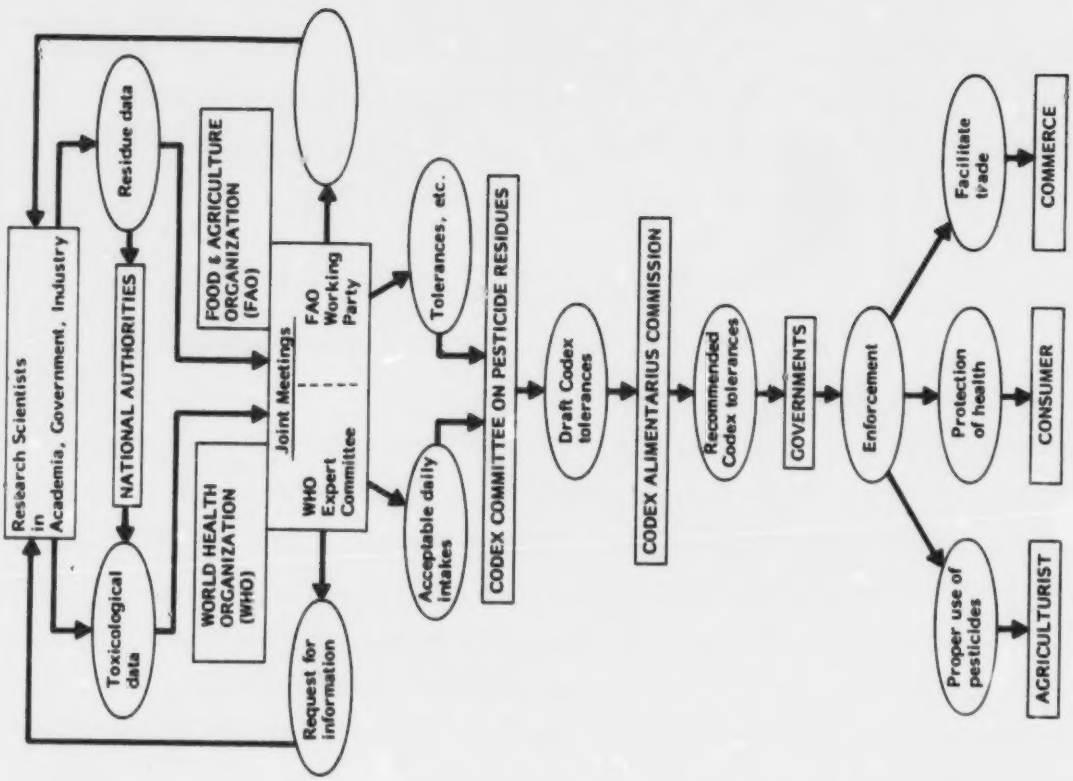
At the meeting, a set of monographs is prepared. Each monograph contains summaries of the relevant data, comments on the data, a toxicological evaluation, and a list of further information required or considered desirable. The toxicological evaluation of a pesticide for which adequate information is available will lead to the establishment of an acceptable daily intake for man. This figure is expressed in terms of milligrams of the chemical per kilogram of body-weight. In cases in which the information is not fully adequate, a temporary acceptable daily intake is established for a period of 3 to 5 years, and the further information that is required is stated. In certain cases, the further information is considered desirable although not essential in the establishment of an acceptable daily intake.

The task of the FAO Working Party is to review the "residue data." This includes the use pattern, the residue resulting from supervised trials, the fate of residues, the methods of residue analysis, and the national tolerances. On the basis of these data, the Working Party recommends limits for residues of pesticides in specific food commodities. The residue data as well as the recommended tolerances are also included in the monographs.

In addition to the monographs, the Joint Meeting also prepares a report during the meeting. The report contains the main decisions and recommendations as well as matters of a general nature. There are, in addition, two annexes: One lists the acceptable daily intakes and the residue limits proposed, and the other lists the further work required or desired. Sometimes other annexes such as a glossary are included to provide additional information concerning specific subjects.

The relationship between the various organizations concerned with the evaluation and control of pesticide residues and the impact on pesticide research are shown in Figure 7. The toxicological and related data, as well as the residue data are provided by research scientists to the national authorities, such as the Environmental Protection Agency. At an international level these data are collected by WHO and FAO for use by the Joint FAO/WHO Meeting on Pesticide Residues. The recommended acceptable daily intakes and the tolerances from the Joint Meetings are transmitted to the Codex Committee on Pesticide Residues, which elaborates draft Codex tolerances. After the views of member states and other international organizations have been received, these are reviewed by the Codex Alimentarius Commission. Following the procedure as described above,

Figure 7


Research Scientists in Academia, Government, Industry
Toxicological data
Residue data
NATIONAL AUTHORITIES
WORLD HEALTH ORGANIZATION (WHO)
FOOD & AGRICULTURE ORGANIZATION (FAO)
Joint Meetings
WHO Expert Committee
FAO Working Party
Request for information
Acceptable daily intakes
Tolerances, etc.
CODEX COMMITTEE ON PESTICIDE RESIDUES
Draft Codex tolerances
CODEX ALIMENTARIUS COMMISSION
Recommended Codex tolerances
GOVERNMENTS
Enforcement
Proper use of pesticides
Protection of health
Facilitate trade
AGRICULTURIST
CONSUMER
COMMERCE

RELATIONSHIP BETWEEN THE VARIOUS ORGANIZATIONS CONCERNED WITH THE EVALUATION AND CONTROL OF PESTICIDE RESIDUES the Codex Alimentarius Commission eventually adopts these tolerances as recommended Codex tolerances. These are then sent by the Directors-General of WHO and FAO to the governments of member states for their consideration for acceptance. Once a government has accepted the Codex tolerance it is then obligated to enforce the tolerance. The enforcement will ensure the protection of the health of the consumer, allow the proper use of pesticides in agriculture, and facilitate trade of food.

In reviewing the toxicological and the residue data, the Joint Meeting may, on the other hand, consider that the information available is inadequate. In such cases the further information required will be transmitted to the research scientists in the industry, government, and universities to promote the development of relevant information.

Dr. FREDERICK WHITTEMORE: I should like to make just one comment with respect to Dr. Lu's description of the work of the Expert Committees and its relationship to the Codex Committee. And that is that at the time the monographs and the reports are prepared by this Joint Meeting, they are sent to all member governments of the two organizations. They are also sent into the Codex procedure, and there was one rather critical figure that he gave there of 103 member governments of the Codex Commission. However, it's my understanding that within the Codex Commission, the member governments which are participating actively in the work of the Committee on Pesticide Residues are a much smaller number, possibly on the order of 45 or 50. This has a rather grave implication with respect to the worlwide scope of these recommendations because many of the governments which are not participating actively in the work of the Codex Committee on Pesticide Residues receive these recommendations from the Joint Meeting and in many instances incorporate these recommendations into their national legislation. This will lead to a false sense of security, so to speak, unless these other recommendations are properly handled through the Codex Committee on Pesticide Residues. There are many countries which are affected by this procedure other than those who are actively participating in the Codex procedure.

DR. F. C. LU: Dr. Whittemore is absolutely correct in his statement that the Codex does not cover all the member states and not all the countries in the world. I did not emphasize this particular point for the simple reasons that first, we're short of time and secondly, I am hopeful that there will be more governments participating more actively in the Codex program.

I remember at the beginning of the Codex program there were only 39 countries and those were practically all in Europe. Now this has been extended throughout the whole world, including all the continents, so that I think the direct influence of the work of the Joint Meeting on the member states will gradually diminish and the importance of the Codex Program will increase. I hope Dr. Whittemore would agree with that.

THE ROLE OF THE FOOD AND AGRICULTURE ORGANIZATION IN PESTICIDE RESEARCH

Edgar E. Turtle, Ph. D. *

I had reservations in accepting the invitation to speak on this subject. This is because the primary task of FAO is to help member countries, and particularly developing countries, in the production of food and other agricultural commodities, whereas the conduct of scientific research is not specifically charged to the organization.

Emphasis On Field Development Activities

Pursuant to these objectives much of the assistance given by the Organization in the control of pests of agriculture during recent years has been through field development projects. These have been funded by the U. N. Development Programme and other bodies and technically supervised by internationally recruited specialists who operate under the general guidance of Headquarters Divisions in Rome. A large part of the activity within these field development projects should be regarded purely as extension or advisory work. The extent to which they are engaged in research varies widely according to the native and immediate objectives of the project.

As examples, there are projects designed to give guidance on the official registration and control of pesticides which include no experimental work; there are projects which fall under the Integrated Pest Control Programme which aim to work up methods for controlling specific pests and to demonstrate the procedures of integrating chemical with biological approaches to the control of pests; there also are projects, such as that for finding acceptable alternative insecticides for the control of locusts in which the activity is entirely research in content.

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*Pesticide Specialist, Food and Agriculture Organization

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This is an area of interest that warrants further study and possibly cooperative action on a national or international basis. Unfortunately we in FAO can only use persuasion to engender work on such items since, until now, we have not been successful in approaches to funding bodies to sponsor research work on such items. Hopefully, the new initiatives covered by the Resolution passed at the Bellagio Conference will cover this problem.

Pesticides in The Integrated Pest Control Programme

Although it would be misleading to list the Integrated Pest Control Programme specifically as part of the "FAO Pesticides Programme," which relates to the programme as set up after the 1962 Conference, it would be equally misleading to omit mention of the programme in any outline of FAO's interests in research with pesticides. This programme was launched at a symposium held in Rome in October 1965. It is supported by a panel of experts formed in 1966, which reviews principles and elaborates procedures for promoting interdisciplinary programmes for the integrated control of major pests based on ecological considerations. Particular attention has been paid to developing procedures on crops such as cotton, on which excessive quantitites of pesticides have often been used. In these developments, pesticides are regarded as components in pest management systems, rather than eradicants of pests as in the older conception. This opens up new perspectives and criteria in assessing the value of new pesticides which, of course, include studies of the advantages and problems involved in the introduction of narrow-spectrum compounds.

For further development of these themes, reference should be made to the various reports of meetings of the expert panel and also to the recently issued report of the Conference on Ecology in Relation to Plant Pest Control held in Rome in December 1972.

The few chemists employed in these field projects are engaged almost entirely in advising on procedures, including laboratory methods for detecting and measuring residues; that is, in helping to provide background technical know-how, rather than in implementing research programmes.

Technical and Research Contents of the Pesticides Programme

These references to field support activities have been located at the opening of this statement to draw attention to their importance in relation to the primary aims and objectives of the Organization. They must be fully taken into account in the formation of lines of policy by the relevant technical divisions.

In their broad principles these lines of technical policy must meet the wishes of the member countries. In the case of pesticides this was first expressed in an intergovernmental conference in 1962. Details of the programme result substantially from consultations with specialists, individually or in meetings arranged for this purpose. These meetings may be of formally established working parties, panels, or committees, or they may be organized on an ad hoc basis.

As for the field projects, the involvement of the expert groups directly in matters of research varies widely from one to another. No group is constituted or funded specifically to undertake or to sponsor research. The following comments indicate the manner in which various ongoing activities engender or stimulate research in the pesticides field.

Of the three Working Parties of Experts set up with the launching of the pesticides programme in 1964, that group on Official Control of Pesticides is charged with providing guidance on registration and other procedures of official control. It has issued general guidelines and is now mainly engaged in issuing standard specifications. This latter activity involves the evaluation of evidence more than the initiation of new research.

The Working Party on Pest Resistance to Pesticides has undertaken a general survey of the occurrence of resistance among agricultural pests. Quite recently it has sponsored a worldwide special survey of resistance to pesticides among post-harvest pests of cereals. It has also provided technical support for a series of publications of standard methods for investigating for the occurrence of resistance in field populations. Currently a new manual on the subject is being prepared by a specially appointed consultant.

The Working Party on Residues of Pesticides has met jointly with the WHO Committee of Experts annually since 1965. It has evaluated data relating to the occurrence and toxicology of residues of some 130 pesticides and made recommendations for acceptable levels in foods for many of them. The recommendations from these Annual Joint Meetings provide the basis for intergovernmental discussions with the Codex Alimentarius Commission.

When the information reviewed by the experts is considered to be insufficient for any scientific or other reason, recommendations are withheld or, with minor deficiencies, are proposed only on a temporary basis. In these instances the nature of the deficiency and the kind of research required is recorded in the published report accompanied by the period after which it is intended to review the position. These periods are set so as to provide a reasonable time for undertaking the necessary research and in the hope that new data will have become available for the subsequent reevaluation. In many instances — and this particularly applies to those in which companies have a continuing patent coverage — additional data have become available and it has been possible to make new recommendations or to remove the "temporary" qualification. In some instances however — and this applies particularly to some of the older common pesticides — new data to meet current criteria have not become available.

These activities have recently obtained encouragement from the U. N. Environment Fund, which is currently supporting a project of preliminary studies which, hopefully, should lead to the wider adoption of these principles in the control of pests in developing countries.

Environmental Impacts of Increasing Use in Developing Countries

It seems certain that increasing quantities of pesticides will undoubtedly be used in developing countries for some years to come. This is partly due to the rapidly increasing demands for food production in the developing countries and partly due to the fact that the introduction of new techniques of pest control and, indeed, of new pesticides is inevitably a fairly slow process. This means that there will be a continuing need to provide support for safe practices in use and for the study of and avoidance of environmental problems where possible.

For some years, we have had ongoing programmes related to the occurrence of residues of pesticides in food. This takes the form of the Annual Joint Meetings of the Working Party on Residues on Food, and support has been given in various projects designed to help developing countries to measure and control residues in their foods. Until recently we have had no funds and no panel of experts specifically concerned with the occurrence of residues and with their effects elsewhere in the environment. Recently, however, the U. N. Environment Fund has accepted our proposal for initiating a coordinated programme aimed in the first instance at investigating possible environmental problems arising from known uses of pesticides in developing countries. We are planning to launch this programme at a meeting to be called in Rome early in 1975.

Future Plans and New Initiatives

What of the future! First, it must be recorded that within the limits of our resources we hope to continue with the above mentioned activities. They adhere to the general objectives set by governments 12 years ago at the 1962

Pesticides Conference. This was to promote safe practices and to raise technical levels of application as a means of taking maximum economic and social advantages while studying problems and taking avoiding actions whenever the need is shown.

At the same time, in the light of the problems still, if not increasingly, being encountered in the control of both agricultural and public health pests, we feel that new comprehensive and coordinated efforts are needed to ensure that the necessary resources are mobilized and used effectively to implement new initiatives for solving pest problems on an international basis. We feel that there is an increasing array of knowledge, in the form of knowledge of ecological requirements for controlling given pests and a variety of new materials. But increased research and practical development resources will be needed if the problems are to be overcome within a reasonable period.

These views were discussed at a Rockefeller Foundation sponsored conference in Bellagio, Italy in April 1974, when proposals were drafted for international coordination of developments in the plant protection area with special emphasis on pesticides and alternative chemical programmes.

The proposal included the suggestion that there should be a secretariat housed with FAO and with units in WHO. It was formally passed to the Director-General of FAO and in July of this year was approved in principle by the FAO Council (i.e., the Governing Body), subject to the need for further elaboration. It is envisaged that this will be done during the coming year. As the proposal, which has been tentatively described as an "International Programme for Control of Pests Affecting Agriculture and Human Health," is open for general examination, it is timely for me to draw your attention to it at this symposium.

The objectives as stated in the original proposal are:*

1. To provide a method of mobilizing in a coordinated way the best world-wide talent in the various specialities related to control of pests of agriculture and human health with focus on developing the soundest programmes and jointly initiating the required actions to solve these increasingly pressing problems.

2. To mobilize the required financial and human resources required for the level of sustained effort required to accomplish these objectives.

3. Provide a means of influencing to the maximum extent possible the policies and attitudes of governments, industries, and the general public to ensure the necessary support and understanding required to obtain the proper implementation of the programmes of pest control deemed desirable.

4. Provide a mechanism for developing the body of knowledge and information required to enable the introduction of chemicals and control procedures into the human environment with an adequate insurance of environmental safety without unnecessary delay and expense.

5. To develop an effective international research network to obtain the necessary information and act as a source of data on the nature of pest problems in the different ecosystems important to man, and evaluate and develop the parameters required for effective control systems.

6. Provide the means for discovery and development to the use stage of new chemicals and devices which fit the requirements of control operations either directly through this programme or in cooperation with the world industries,

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*Taken from the program proposal adopted by resolution at the Bellagio Conference, April 1974.

and provide the means for licensing or assisting industries on a mutually advantageous basis to introduce products useful in pest control which would not normally be developed by unassisted commercial endeavor.

7. Stimulate research on products and devices now in common use to determine how they can be used more efficiently and safely in pest control programmes.

8. Provide the basis for a training network which can provide the number and quality of people trained adequately to provide the required manpower for the various components of pest control programmes from research to operational aspects.

9. Provide a source for obtaining consultation and suitable personnel for technical assistance programmes being provided for governments and to provide assistance to industries for obtaining the information required to make sound decisions.

10. Provide mechanisms to ensure maximum rapid exchange of information and personal discussion among and within the various groups dealing with or dependent upon pest control.

The organizational structure is also referred to in the following manner:

> The programme is designed to provide an international secretariat operating under the authority of a governing board to develop with the assistance of a series of advisory committees comprehensive and coordinated programmes to be carried out through research contracts and agreements or other procedures to implement coordinated programmes in the fields of pesticide toxicology, pesticide chemistry, physiology and biochemistry, environmental impact, international registration standards, and appropriate biological groups designed to develop the requirements for the type of basic pest control programmes required.
>
> In each of these areas programmes may include research, training, technical assistance and advisory or consulting services.

Developing methods to expedite the rapid exchange of information should be included in the responsibility of the programme.

The secretariat would be comprised of an executive secretary and coordinators for each of the programme areas. The programme budgets and activities including the secretariat would be the responsibility of a governing board. The programmes and budget proposals for each of the areas would be developed by advisory committees working with the area coordinator. A key element in the programme development and evolution in each area would be an annual meeting of participants in each area to present their findings to the advisory committee and assist the advisory committe in development of programmes and budgets.

In addition to these various programme areas, there would also need to be facilities to handle patents, contracts and licenses.*

From the above indication of the present discussional status of these proposals, it is obviously not possible to give you any firm assurances regarding the future programme of our Organization in this field other than a continuation of that covered by the earlier part of this paper.

Finally on behalf of FAO, I must express our grateful thanks to the Environmental Protection Agency for the invitation to this symposium, both for the purpose of hearing of the plans of the Agency and of being able to present this paper on our programme. Although the implementation of our intentions must be contingent on our obtaining the necessary funding resources, I can assure you as a staff member of the Plant Protection Service of the Plant Production and Protection Division, that we do propose to press our efforts along the lines indicated.

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*Program proposal adopted by resolution at the Bellagio Conference, April 1974.

U.S. PARTICIPATION IN CODEX

Lowell E. Miller*

The Codex Alimentarius Commission came into being in 1962, 12 years ago. In 1963 the Commission, at its first session, established the Codex Committee on Pesticide Residues (CCPR) with the responsibility to propose international tolerances for pesticide residues in specific foods. Since that time, the CCPR has met in seven sessions, the last in February 1974.

There are now about 1,000 proposed tolerances at some stage in the Codex process. Approximately 100 of these have been formally submitted to member countries for acceptance. Another 140 proposed tolerances will soon be recommended to member countries for acceptance as a result of the actions taken at the July 1974 meeting of the Commission. Obviously, the wheels of Codex have been grinding.

Yet today in 1974 blunt questions are being asked about the future of Codex. Questions such as: Will Codex "get off the ground"? Will Codex live up to its high promises? These questions are prompted, I think, by the fact that while a great many tolerance proposals are in the Codex process, the Codex pesticide residue work has yet to produce observable results; Codex has not yet demonstrated that countries will agree to or accept a significant number of pesticide residue tolerances.

It goes without saying that the United States has a great concern for the future of Codex (and when I refer to "Codex," I want to make clear that I am referring to the work of Codex as it relates to the establishment of international tolerances for pesticide residues in foods). The United States has always strongly supported the principles of the Codex Alimentarius Commission. We have also

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voiced strong support for the work of the CCPR. But we have never really come to grips with certain key questions which must be answered before we can fully participate in the Codex work.

And we in the United States are not alone in this situation. I find that the questions we have been trying to resolve are the same questions being grappled with in other countries.

I do not intend this morning, however, to talk about the participation of other countries in Codex. Rather, I would like to discuss U.S. participation in Codex — specifically, to identify the questions and to discuss what we have done to answer these questions and where we go from here.

First of all, a few background remarks about Codex:

The Codex Alimentarius Commission is an international body concerned with the development of international food standards, including maximum limits for pesticide residues in food. The Commission was established to implement the Joint Food Standards Program of the Food and Agriculture Organization of the United Nations (FAO) and the World Health Organization (WHO). Membership in Codex is made up of those members of FAO and WHO who have notified the organizations of their desire to be members of Codex. At present, approximately 100 countries are members of Codex.

The purposes of the Commission, broadly stated, are to protect the health of consumers and to ensure fair practices in the food trade.

The work of the Commission is carried out through various committees, each chaired by one of the participating countries. A number of Codex Committees have been established to elaborate standards for various major food commodity groups (e.g., milk and milk products, fats and oils, sugars, meats, fish and fishery products). Other committees deal with particular problems associated with the commodity groups (e.g., food additivies, food labeling, food hygiene, methods of analysis and sampling, pesticide residues).

Maximum residue limits for pesticides (tolerances) are developed through a 10-step procedure. This procedure gives member countries an opportunity to review and comment on tolerance proposals at various stages of the process. In essence, there are three distinct phases of the Codex work.

FAO/WHO Joint Meeting

The principal scientific work is carried out by experts appointed by the Directors-General of FAO and WHO and is supported by a permanent secretariat. The experts come together in an annual meeting (Joint Meeting) to discuss the results of their evaluations of assigned compounds and to prepare appropriate recommendations. Chemicals are reviewed by the Joint Meeting on the basis of priorities recommended by the Codex Committee on Pesticide Residues. Toxicological and residue data and information on appropriate methods of analysis may be submitted to the Joint Meeting from any country. The Joint Meeting, upon the basis of the information available, proposes tolerances, temporary tolerances, or practical residue limits for the pesticide. A monograph on each chemical is prepared by a member of the Joint Meeting. In addition, reports of the Joint Meetings are published. These reports, together with an abbreviated version of the monographs, set forth the bases for the Joint Meeting proposals.

The Codex Committee on Pesticide Residues (CCPR)

The CCPR provides the forum for discussions among countries on the proposed tolerances. Countries are invited to submit written comments on the proposals at steps 3 and 6 of the Codex procedure. The detailed consideration of tolerance proposals and written comments, however, occurs at the CCPR sessions. At CCPR sessions, countries are expected to indicate concurrence or nonconcurrence on each tolerance proposal. It was made clear at the last session of the CCPR (February 1974) that in cases in which a country did not concur with a proposal, that country was expected to give a specific reason for the nonconcurrence. It was also made clear that a different national tolerance, in itself, was not considered a sufficient reason for nonconcurrence. Countries are expected to give the basis for any objection supported by data.

Commission Recommendations for Acceptance

The end result of CCPR work is the forwarding of tolerance proposals to the Commission with recommendations that the proposals be submitted to member countries for acceptance as international tolerances. When the Commission concurs with CCPR actions (step 8), the proposals are formally submitted to member countries with the request that the Commission be notified of their acceptance in accordance with the General Principles of the Commission (step 9).

It is at this point that we come to the core question in the establishment of international tolerances: What is meant by "acceptance" of a Codex proposed tolerance? Asked another way, what commitment does a country make when it "accepts" a Codex proposal?

But these are questions which are not only relevant to the end step of the Codex process when proposals are formally submitted to countries for acceptance; these are questions, it seems to me, which must be resolved before a country is in a position to give full consideration to a tolerance proposal at the earliest step in the Codex review process (step 3). How can a country determine what its position is with respect to a proposed international tolerance at any step until it has also determined what "acceptance" of such tolerance means?

The Codex General Principles define "acceptance" and set forth the procedures for the acceptance of Codex proposals. At the last meeting of the Codex Alimentarius Commission, held in July 1974, a new and separate acceptance procedure was established for pesticide residues. Under these procedures, there are three types of acceptances.

1. "Full acceptance" which means that a country agrees to apply the Codex tolerance to both imported and domestic food.

2. "Limited acceptance" which allows a country to apply a Codex tolerance to imports only. Under "limited acceptance," however, a country may not apply a more stringent (lower) tolerance on imports. This is a new type of acceptance and is intended to make it easier for countries to recognize good agricultural practice in another country. It also makes it clear that a country may (a) recognize a higher tolerance for imported food than for domestic food and (b) accept a pesticide residue tolerance on imported commodities while, at the same time, it restricts or prohibits the use of the pesticide in its own country.

3. "Target acceptance" which allows a country to indicate its intention to give full acceptance or limited acceptance to a Codex tolerance after a stated number of years.

In the United States, there are three agencies which are vitally concerned with the Codex acceptance procedures — FDA, USDA, and EPA. EPA would seem most heavily involved since EPA has the responsibility to establish pesticide tolerances under our national statutes. FDA and USDA enforce these tolerances. USDA is also concerned because of its responsibilities for foreign trade in agricultural commodities.

In recent months, representatives of these three agencies have had discussions concerning the U.S. position on acceptance of a Codex tolerance. Two basic tenets have emerged from these discussions:

1. Before a Codex proposed tolerance may be accepted, it must be determined that the Codex tolerance fully complies with the requirements of our national law and a regulation establishing such a tolerance must have been promulgated. In short, the establishment of a tolerance under national law is a condition precedent to our accepting a Codex tolerance.

2. At present, we will not operate on a so-called two-tolerance concept; that is, we will not establish differing tolerances for imported and domestic foods. However, we do not want to foreclose the possibility of considering the establishment of a different tolerance for an imported commodity in a specific situation if circumstances warrant.

The application of these tenets to our Codex tolerance review work seems clear.

We in EPA will review each proposed Codex tolerance to determine whether it complies with the requirements of U.S. law, giving full recognition to the U.S. position, as stated at the last meeting of the Commission, that the United States will strive to give "full acceptance" to as many as possible of the proposed tolerances recommended by the Commission for acceptance.

When the Codex recommended tolerances differ from established U.S. tolerances, we will review each proposal from the standpoint of determining whether changes can be made in the U.S. tolerance level. In all possible cases, action will be initiated under U.S. statutes to make the U.S. tolerances consistent with the Codex proposals. When the United States cannot accept a Codex proposal for reasons of good agricultural practice in this country or for human health reasons, the reasons for our nonacceptance and the data upon which our decision is based will be fully set forth.

We also support the principle that would allow a country accepting a Codex tolerance to apply such tolerance to imports only, while prohibiting or restricting the use of the pesticide domestically. We will follow this principle. It is important to recognize that the establishment of a tolerance for a pesticide chemical and the registration of the pesticide for use are two related but separate actions.

Codex proposed tolerances fall into four categories as they relate to U. S. tolerances:

1. The Codex proposed tolerance is the same as an established U. S. tolerance. Here, of course, there is no problem and we can accept the Codex proposal without further review. The United States has formally accepted those Codex tolerances now at step 9 that correspond to U. S. tolerances.

2. The Codex proposed tolerance is lower than the U. S. tolerance. Here the question is one of analysis of all available residue data to determine whether the U. S. tolerance can be lowered in accordance with good agricultural practice in the United States.

3. The Codex proposed tolerance is higher than the U. S. tolerance. Here the question is one of safety. In my opinion, the United States must be willing to raise U. S. tolerances to a higher Codex level if such can be supported scientifically. The United States cannot accept only those Codex tolerances which are equal to or less than a U. S. tolerance. If we expect other countries to recognize good agricultural practices in the United States, we must do the same in the absence of a determination that the higher tolerance cannot be justified for human health reasons.

4. The proposed Codex tolerance is for the residue of a pesticide not registered for use in the United States. Here as indicated before we can and, as a matter of fact, have established tolerances even though the pesticide is not registered for the use in question in the United States.

Finally I would like to make some personal observations:

While Codex has been criticized for its cumbersome procedures and for its lack of visible accomplishments, I believe that significant work has been done in the CCPR in the last few years. The problems have been identified and discussed; differing views have been aired; a real effort has been and is being made to make the work of Codex more effective. I believe that we will see real progress in the work of Codex in the years immediately ahead.

I am, therefore, optimistic about the future of Codex. I say this for two reasons in addition to what I have just said. First, I believe there is a realization in all countries that we are, in the words of one CCPR delegate, at "pay day." Countries can no longer dodge the question of formal acceptance of an international tolerance; we are being forced into demonstrating what our commitments to the principles of Codex are. Second, I came away from the last session of the CCPR with the distinct feeling that it was the mood of the session that Codex must work and that it can. This feeling was in large part due to the firm and able leadership of our Chairman, Dr. Pieters of the Netherlands. It was also due to the expressions of many of the delegates with whom I talked, that the objectives of Codex can best be achieved on a global rather than regional basis and that national policies with respect to the regulation of pesticides should not present irreconcilable differences with the objectives of Codex.

QUESTION: Is there not a basic difference in what Codex calls a tolerance and how we establish our tolerances in terms of the residue base data? That is, we are required to establish tolerance based on the highest residue levels that we find in a prescribed try. Now I get the impression — I can't remember what they call it in Codex, you probably will — that that's not necessarily the case for international tolerance. Is the number that is quoted necessarily representative of the absolute maximum when used as directed?

MR. LOWELL MILLER: We could have a long discussion about the differing philosophies in the so-called high-tolerance and low-tolerance countries. Part of the difference arises because of our law. Our tolerance procedures are mandated by statute. Under our law, any food that exceeds the tolerance level is adulterated. In my opinion, we cannot establish a tolerance on a mean batch concentration and excuse violations that are over that mean. But this is a philosophical question which I don't think we have time to get into right now. We can discuss it later.

QUESTION: Mr. Miller, I recall a comment from you and also Dr. Lu with regard to accepting tolerances based on domestic production as well as import, but neither of you commented on considering these same tolerances with regard to exported foods and it seems to me this is a very important picture.

In exporting from here to Europe there may be no problem, but in many cases we are exporting to the lesser developed countries where frequently they have no ability to monitor and the like. Yet it seems to me that we should be establishing the same sort of levels in enforcement in export as well as import, although this may cause a little problem as far as control in monitoring.

MR. MILLER: If I understand your comment, this is one of the big advantages, as I see it, of the Codex work. One of the main advantages is that developing countries which do not have the expertise to do the work themselves get the advantage of the Codex work.

SOME PREREQUISITE CONDITIONS FOR THE DETERMINATION AND EFFICIENT REALIZATION OF THE ALTERNATIVE CHEMICALS PROGRAM IN SOME EUROPEAN AND DEVELOPING COUNTRIES

Radojica Kljajic*

Introduction

I deeply appreciate the honour that has been conferred upon me by the invitation from the Environmental Protection Agency (EPA) to deliver this presentation, with the opportunity thus provided for a free expression of views upon some fundamental aspects in connection with pest management and the rational use of pesticides, i.e. the Alternative Chemicals Program.

Dr. John Buckley said yesterday that we did not start from zero, namely from the beginning in the field of the rational use of pesticides. He's absolutely right, but how great are the varying distances from zero in different countries? In the United States, like most developed countries, the distance from zero is much greater than the distance from zero reached in non-developed countries.

Due to the time limit, I would like to draw your attention to a few questions, starting with definite problems that have been worrying most of the European countries, as well as some of the developing countries. First and foremost, from my own country which has very different climatic conditions, different types of soil, and by its economic progress presents the picture of "a miniature world." In this respect, most of the problems, as well as the means of solution, are different or of a different character. Because the problems are numerous, exceptionally complex, and interrelated, their solutions must have an organized and constant character, and realization of the procedures must be coordinated by united action. Depending on the problem, the action should be of local, regional, national, and/ or international character. The rational use of pesticides and environmental

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safety has become an everyday preoccupation bothering so far not only the scientists, producers and applicators of pesticides, competent specialists and responsible government officials, but also the whole community.

Why the Alternative Chemicals Program ? Is it because of a few persistent insecticides, or because compounds ten times as expensive should replace them, or because we are not quite sure what should be used as replacements ? Could the reason be very high toxicity or inadequate efficiency, or the unknown long-term effects, or the existence of a great number of alternative compounds with a high number of formulations, or some other reason in the chain of dilemmas. The problems with pesticides are so innumerable and so constant that both the public and certain specialists often make statements such that pesticides should simply be prohibited or that very soon their replacement might be expected by other "harmless" methods.

It is difficult to escape the impression that due to the pressure of non-informed persons or due to our desperation to achieve some immediate effects, we often lose the basis for objectivity. We direct our activities mainly to the consequences and not to the causes of the basic and fundamental problems, although being important factors of contemporary mankind they strike us directly.

Pesticides and Food, Feed, and Fiber

Topping the list of mankind's problems today is the provision of sufficient quantities of food and other vital needs for a constantly increasing population. To be sure, food has been the greatest of man's preoccupations from the remote ages. It has been the potential motive for all disagreements, disputes, conflicts, and ruins of many nations. The fact that there are nearly 2 billion starving or food-deficient humans is overwhelming. This number equals the total world population of 50 years ago. Although in the developed countries it appears as if hunger has disappeared, it has never so expressly threatened humanity. There are only 10 countries with an excess of food supplies, the United States with approximately 50 percent. The perspective of further food deficiency during the coming years — there will be about 7 billion people — is no less fantastic than a vision of an increasing abundance.

In short, when we talk today about an energy crisis, thinking first of oil, we must not neglect to consider the significance of the shortage of food, another important source of energy. This should be particularly stressed because the total area on which the world population exists is mainly constant which means that production will have to be intensified by all available means, and we will have to recognize that the byproducts and uncontrolled application of some production means may imperil the existence of man.

To what extent the solution of these problems could be simplified depends primarily on the direction of mankind's efforts. In particular it depends on its scientific, technical, and technological achievements, as well as on the engagement of all social and economic factors which may contribute to any extent toward an organized solution, such as this Symposium.

Various pests actively and persistently cause a decrease in food production by one quarter, one third, or even one half or more. That means that every fourth, third, or second farmer works for the existence of such pests. In fact, they represent the only "competitors" to humanity in the production and utilization of raw materials and the production of other goods. Their constant presence during the process of production, storage, and traffic drastically decreases an enormous food potential.

For these reasons, pest control has the character of a constant and continuous fight, with man and numerous useful organisms on the one side and over 15 thousand harmful biological agents on the other side. In order to lessen the losses in this continuous "battle," man has been employing the most up-to-date scientific, technical, and technological achievements. Man does so not only to diminish the quantitative and qualitative losses, but also to fight the insects, rodents, and other pests in urban settlements and recreational localities.

Due to the fact that the "enemy" acclimatizes to new conditions, man is also forced to develop his strategy and tactical measures and weapons against pests, keeping in mind the presence and necessity of saving the normal growth and development of a great number of useful organisms within various ecosystems.

Chemical Methods as Part of the Other Pest Control Methods

The thesis on eradication of harmful species cannot be accepted as a scientific basis. In most ecosystems, some harmful species are always present. Any measures applied in agriculture, forestry, animal husbandry, food industry, hygiene, urban settlements, and recreation centers directly or indirectly affects biological agents, thus intensifying or preventing their appearance and harmful effects.

Therefore, numerous and different methods have been applied in this respect which can be grouped as biological, mechanical, physical, and chemical.

Biological Methods

These include the selection and/or creation of resistant varieties of species and the regulation of their cultivated growth in order to remove or to inhibit the appearance and spreading of pests. In some cases antagonistic phenomena produced in the laboratory or industrially are used against individual enemies – predators, parasites, and their metabolites.

It is usually understood that under biological methods only part of the definition, the creation of resistant varieties, is considered. I believe, however, that this is inadequate and scientifically untenable, since the selection and creation of resistant species and hybrids in plants and animal species, as well as the regulation of their cultivation, is being widely applied with exceptional significance.

Logically, in such cases failures are possible but they should not be exaggerated and their positive effects should not be neglected. In cases of antagonistic phenomena, reverse actions should be undertaken. Since practical application is not as widespread at present as the use of resistant species, potential effects of placement in ecosystems could be exceptionally significant. The question is in genetic manipulation, which could be more dangerous for ecosystems than some toxic or persistent pesticides.

Mechanical Methods

By man's activity and the use of certain tools and technical means, biological agents may be directly destroyed, ecological conditions made unsuitable for their development and propagation, or in the case of their appearance, their harmful effect diminished.

This group of methods has been widely applied and is found to be of exceptional importance in a variety of areas including soil preparation, early planting of crops, destruction of crop residues, tillage, destruction of volunteer plants, mechanical harvesting, etc.

Similar to crop residues after mechanized picking, all other measures and procedures, as well as solid waste accumulation and bad sanitation conditions in urban settlements can be the source and/or stimulus for propagation of rodents, insects, and other pests.

Physical Methods

By means of electromagnetic waves of different energy, i.e., thermal, electric, sound and ultrasound, visible and ionizing radiations, direct or indirect control is being carried out, or at least such ecological conditions are realized in which harmful organisms cannot develop.

The opinions related to this group of methods are often different, resulting in underestimation and neglect of their significance and role. They are rather widely represented by disinfection; sterilization; pasteurization; temperature regulation in storehouses, cooling houses, and refrigerators; moisture regulation, etc.

Chemical Methods

By means of the application of different compounds and their combination, pests may be controlled either directly or indirectly. Since mechanical methods and most of the biological and physical methods are actually agrotechnical, zootechnical, or some other measure or procedure which does not guarantee success, there is a necessity for intervention by chemical methods.

It should be emphasized that the further progress of science, techniques, and technology will contribute to the discovery of some new methods and to the development of the existing ones in all four groups of methods. Only by correct choice and application can these give, with the least effort and risk, the most benefit. Accordingly, each of these methods, including chemical, must be rationally applied, as should be the case with other achievements of mankind.

Choice of Pesticides and the Alternative Chemicals Program

Certain benefits in food and other goods production, as well as successful vector control could not be imagined without pesticides. However, the protection of food stocks and other goods with poisons is a two-edged sword, which is very efficient in the hands of instructed, trained people, both otherwise very dangerous or even fatal. Isn't this also the case with other numerous achievements of our civilization?

The general impression is that our activities, especially in some European and developing countries, have not been adequately concentrated in this direction. We have probably been occupied too much and too long with discussions on DDT and other persistent insecticides, although it is somehow logical, as they are persistent and their pathways can be relatively easily traced. Meanwhile, what about the hundreds of other compounds and potential problems which are present or ready to appear with their short- or long-term effects, which are of exceptional importance for their choice and application. They are easily diluted, less persistent, and more difficult to trace, but this does not mean that exponential consequences of pollution of the air, water, soil, and living organisms and the effects on some ecosystems are automatically solved. Beyond numerous papers on this subject, our knowledge is sparse and not really adequate. Let me mention the problem of resistance.

It is a well known fact that all living organisms have the ability to adapt to changed environmental conditions. This is actually the basis of the evolution of living organisms. Accordingly, resistance is a general biological phenomenon and the intake of toxic matters including pesticides into the biosphere is a significant ecological factor. Resistance, up to the present, has been established in insects, mites, fish, rodents, pathogens, and weeds. The acquired and inherited properties are in question. In this respect, the phenomenon is exceptionally complex, not only from the scientific but also from the practical point of view. On this occasion I will mention only three examples:

It is known that the potato beetle, Leptinotarsa decemlineata, after 7 to 14 generations multiplies its resistance to DDT 10 times in comparison to a normally sensitive population. It has been evaluated that control is not efficient if the index is higher than 3.

In my Department, the resistance of the Colorado potato beetle to 6 insecticides was investigated in Yugoslavia, and it was established that the index approximates 88.2, namely the ld-p line runs up to 1.47 in normally sensitive and up to 0.69 in highly resistant populations. Our laboratory experiments showed that the resistance index in resistant populations was as high as 389.

In the house fly, Musca domestica, the resistance appeared after 30 generations. During the following 41 generations it is unchangeable, and after that it gradually decreases. Even in this case the genetically disturbed population becomes rapidly resistant to new insecticides. However, the problem is even more complex owing to the possibility of cross- and multi-resistance.

The ancient dream of the plant pathologists and agriculturists was to get systemic fungicides. This has finally been achieved. The problems of serious resistance were not known before in this field. Recently, there have been cases that after 1- or 2-year applications of certain compounds, some resistant biotypes appeared. For example, powdery mildew, Sphaerotheca spp, to Ethrimol, a number of species, including Botrytis spp., to Benomyl, and similar cases. These phenomena may have serious implications. Therefore, in the planning and realization of the Alternative Chemicals Program, due attention must be paid to the problems of resistance such as early detection, previously checked introduction of new compounds in determined fields, constant control and timely replacement with other compounds, and successive application.

It is important to stress that the application of some other chemical methods such as the application of attractants, repellents, bait, sprays, juvenile hormones, etc., carries in itself certain complexities and potential complications which make us responsible not only for application, but also for propagating the perspectives and orientation.

Factors Influencing the Efficiency and Toxicity of Pesticides

The rational choice of alternative chemicals cannot be realized without an awareness of the basic factors influencing the efficiency and toxicity of pesticides.

Namely, the complex and complementary activity of pesticides may be stipulated or it may have a reflexive effect with the whole series of factors of abiotic and biotic character.

In order to be cognizant of the complex action of pesticides and to minimize contamination of the air, water, soil, and living organisms, as well as to achieve the most successful suppression of harmful organisms, it is necessary, at least in short, to point out the basic groups of objective factors. This is important because it could help in the work of establishing the causes and no less in determining the consequences of a non-rational application of pesticides.

Among the factors on which the synchronized program of the application of pesticides should be based are the following:

1. The basic characteristics of plants and animals, such as the genotype and phenotype characteristics of the species, varieties and hybrid plants, namely, the species in all stages of growth and development essentially affect the ripening, adhering, retaining,and degradation of pesticides on the surface of an organism. They affect as well the degree of penetration, translocation, decomposition, and transformation into other compounds, which are sometimes even more toxic than the pesticides themselves.

2. Pests react specifically to the activity of pesticides because of the various phenotype and genotype characteristics of each species or its lower biological category in all stadiums or development phases. The choice of pesticides must be scientific as well as its concentration, the applied amount, and the method of application. This is especially important in regard to the need to know its mode of action and the appearance and disappearance of resistant forms.

3. Physicochemical and technological properties of pesticides (the structure of the active substance and ingredients, their compatibility, solubility,

evaporation, hygroscopy, viscosity, the size and shape of particles, electrostatic potential) have an impact upon the dispersion of pesticides in space and upon the specific toxicity toward each pest individually or an entire plant species.

4. Mechanical and technical characteristics of equipment (e.g., motion, speed, effectiveness of mixing suspensions and emulsions, the construction and shape of dispersion, pressure, velocity of particles, equipment temperature, and other characteristics) act on the uniformity of pesticide dispersion in space, pesticide effectiveness, and toxicity.

5. Climate and microclimate factors — air represents the largest part of the environment around the organism we are protecting, the biological agents we are holding back, and the pesticides we are applying. Therefore, humidity, temperature, air speed and direction of movement, and atmospheric pressure have a great effect on both the dispersion and the dynamics of degradation and transformation, as well as on the growth and development of cultivated organisms and pests.

6. Soil is the basic recipient of the direct or indirect stocking of pesticides. Its characteristics, such as pH value, contents of organic matter, sand, clay, ion-exchange ability, biokinetic relations, and others, also have a complex impact both on migration and degradation of pesticides, i.e. the degree of their toxicity, and on the growth and development of plants, various useful organisms, and pests. Although the above factors are presented in my paper separately, they are nevertheless necessary to mention in regard to efficiency and toxicity, and therefore have to be adequatly treated and solved.

For a clear understanding of these numerous factors which are very complex and interrelated, we can use a layman's interpretation by introducing symbols.

The production, distribution, and application of each pesticide may be regarded as the "movement of a vehicle" along a traced road from the industrial production, stocking, distribution, application in protecting the food fund (food, feed, and fiber), from preparing seeds and soil to the harvest or picking time respectively, then to stocking, manufacturing, and consumption. The "vehicle" moves in definite forms to the organism that is being protected, where it stays for a short time, holds the existing pests back with more or less success, sometimes even affects the living processes of useful organisms, turning them into other forms, interacts with other compounds, decreases or increases toxic properties, and/or continues its "trip" through the plant and animal products and water to man.

Since these traced roads or rather "road networks" are jammed with a large number of completely different pesticides and related compounds in the environment from other sources with which they can interact, the creation of "roads" and "vehicles" must be scientifically elaborated and constructed of good materials. At the same time, traffic regulators must be entrusted to trained and qualified persons who will work and study hard and constantly, and pay full respect to all engaged, irrespectively of the "section" they are in. The activity of the "traffic" must be based on synchronized, regulated, and coordinated programming. Otherwise, the "trip" of pesticides will have to follow either an unfinished "network" or only certain "sections" using bad "vehicles" and will become a "traffic chaos."

Importance of Education

Although we are generally aware of the great importance of education, there is an impression that we do not have enough strength or that we do not pay enough attention to these problems.

We are witnesses or participants at numerous national and international meetings in Europe and with United Nations Agencies and are exposed to a great number of scientific publications on general or very specific scientific problems, which is exceptionally positive. However, this is not the case with education problems. The work to reform our educational plans and programs concerning all the grades of education, has not yet found its adequate place. But the consequences are man-sized. I shall quote some examples. The application of herbicides increases from year to year. In Yugoslavia, for example, it has increased more than five times in the last 10 years (1964-1973). In Finland in 1973, herbicides made up 90 percent of all applied pesticides in active ingredients. Also, in this country, the monetary value of herbicides sold was 58 percent, that of insecticides, rodenticides, etc. was 36 percent, and the value of fungicides was 6 percent. The proportion of herbicides increased continuously, being 20 percent in 1957, 38 percent in 1963, and 50 percent in 1968.

Illustrations similar to those in Yugoslavia and Finland could be quoted from other European countries as well. However, because of the main orientation on the problems of insecticides, especially on persistent ones, our knowledge about the potential short-term or long-term effects of herbicides is absolutely insufficient. Among the non-informed people the idea has been formed that herbicides are almost completely harmless and that they cannot have visible bad effects.

From year to year, there is a constant increase in the consumption of pesticides by town inhabitants in gardens, small fields, as a hobby or extra earning, in flats, recreation centres and other places. How much do they know about pesticides? Often not very much or nothing. There are even tragicomic cases when some people use spray in order to kill only 1 or 2 flies, mosquitoes, or some other insects to protect a few pots of flowers, or to spray the bedroom, bed linen, and what is even worse, their own body, to protect themselves from the mosquitoes.

With regard to the fact that the population is very heterogeneous according to the degree and profile of education, they are often inclined to experiment and to introduce innovation, but they underrate invisible danger at the moment. Therefore, their training is more complicated than that of applicators, users, and farmers whose lives directly depend on production. The production in which the pesticides are used, such as vineyards, amounts to 35 to 40 percent of annual expenses.

It is hard to expect, however, more prominent progress in the field of education, as the students of agriculture as well as forestry gain little information about the prerequisites of the rational application of pesticides and even less on environmental safety. The students of medicine, veterinary science, economy, law, sociology, etc. are informed about this even less.

A special problem during education is an insufficient humanitarian base of professional orientation. That is why with some future specialist there is an intensified craving for material effects, often only for a short period. This short sightedness and this blindfolded egoism which is governed by the motto "after me a disaster," could present irreparable damage to the ecosystems in which the man lives.

Finally, it is necessary as quickly as possible to pay maximum attention to educational problems from the point of the rational use of pesticides and environmental protection and safety. This should be carried out at all levels, from kindergarten children to post-doctoral students, including various short courses for the education of adults regardless of their function — parliament, government authorities, university professors and teachers, journalists, lawyers, medical doctors, and others if their activity has or can have any influence on solving the problems of the rational use of pesticides and/or environmental safety.

It is an old proverb "better prevent than cure" and that holds good for pest management and the rational use of pesticides too.

DR. ARNOLD ASPELIN: I would just like to comment on the need for a broadened, multidisciplinary approach to the international efforts such as have been discussed today. Throughout these sessions I've gotten the feeling that social and economic values were not addressed very squarely. Maybe this was done subconsciously or even consciously in some cases. It is not too difficult for me to understand why we can't get agreement among nations on numbers such as under Codex. Economists and other social scientists might well be able to provide some useful insights into some of these issues which apparently are being handled mostly by physical and life scientists who early on got into the pesticides area. So I would just like to make an appeal for a broader social science approach to some of these things.

Dr. CHARLES KRISTER: Professor Kljajic, since you brought it up, I'd like to take advantage of the opportunity to extend either your comments or perhaps clarify some of the remarks about benomyl. Was this a laboratory test in which resistance occurred, or was it actually resistance out in the field? Was this a field plot where resistance occurred or was it a laboratory screening in which resistance occurred?

DR. RADOJICA KLJAJIC: The cited examples have been taken from the literature and are related to the results obtained both in vitro and in vivo.

DR. KRISTER: Two comments that I would like to offer. One is that in our experience out in the field where resistance has occurred, the resistant organisms were actually there in the field. Secondly, where there has been problems in connection with use of benomyl on any particular crop, the resistance can be handled by a combination of maueb and benomyl, or alternate treatments of benomyl and maueb. Does this confirm what has been found in your experience?

DR. KLJAJIC: The cited examples, including benomyl, are illustrations of the complex and complicated problems of the resistant pests not only to the "first" but also to the "second" and "third generation" of pesticides. My point was that the application of every new and old compound must always be under continuous scientific supervision.

NATIONAL ENVIRONMENTAL PESTICIDE MONITORING PROGRAM

Dr. William S. Murray*

Under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) as amended, the Environmental Protection Agency (EPA) is responsible for designing and implementing a National Pesticide Monitoring Plan. A plan is currently in the review stage, but an existing National Pesticide Monitoring Network has been operating for several years and is coordinated by an interagency body called the Monitoring Panel of the Federal Working Group on Pest Management. In addition to EPA, the agencies represented on this panel are the Food and Drug Administration which is responsible for monitoring food and feed, the Department of Agriculture which is responsible for monitoring red meat and poultry, the Fish and Wildlife Service of USDI which monitors freshwater fish and various birds, and the Department of Defense which has its own monitoring program on military reservations.

The other environmental components are being monitored by the Environmental Protection Agency. They include air, fresh water, estuaries, the oceans, soil, crops associated with the soil, and human tissue. These programs are the direct responsibility of the Ecological Monitoring Branch in the Technical Services Division of the Office of Pesticide Programs.

During this talk, I will describe our monitoring systems and special projects capability.

All monitoring systems operate through three basic phases:

- Field collection of the samples
- Laboratory chemical analyses of these samples
- Analysis and interpretation of the data

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I will use the National Soils Monitoring Program to describe each of these three phases and then only describe the field collection phase for the remaining systems, since that is the only different phase among the programs.

The National Soils Monitoring Program

The National Soils Monitoring Program was designed to collect statistically valid samples from the nation's cropland, noncropland, and urban areas. A total of 13,300 sites in the cropland and noncropland areas were identified, with 1/4 of this number to be sampled each year. The design proved too ambitious for the available resources and noncropland is no longer sampled. The number of cropland sites sampled since the program was instituted has ranged from 1500 to 1700 per year. Since the program has not been able to consistently cover the whole nation, a new modified design will be developed for FY 1976. To date, cropland soil has been sampled in 45 states;* noncropland soil has been sampled in 28 states;** and 37 standard metropolitan statistical areas have been sampled for our urban soil monitoring program (Figure 1).

Soil samples are collected using a soil core 3 inches deep by 2 inches in diameter. A cropland sampling site is usually made up of 10 acres with 50 soil cores collected over that 10 acres on a 5 x 10 grid. In the urban areas, this is modified to use a 50 x 50-foot plot and a 4 x 4-grid.

After the soil samples have been collected, they are screened three times through 1/4-inch mesh screening and a 2-quart subsample is taken. Equipment is carefully washed to ensure that there is no possibility of cross-contamination between sampling sites. For each site a map is made to enable us to go back to

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*All but Montana, Kansas, Texas, Alaska, Hawaii

**All but Alabama, Arkansas, California, Colorado, Florida, Louisiana, Minnesota, Mississippi, Missouri, Nevada, New Mexico, North Dakota, Oklahoma, South Carolina, South Dakota, Utah, Oregon, Montana, Kansas, Texas, Alaska, Hawaii

Figure 1

Urban Soil Sampling Sites

FY 70
Bakersfield, Ca.
Camden, N.J.
Houston, Tex.
Manhattan, Kan.
Miami, Fla.
Milwaukee, Wis.
Salt Lake City, Utah
Waterbury, Conn.

FY 71
Mobile, Ala.
Wilmington, Del.
Honolulu, Hawaii
Sioux City, Iowa
Augusta, Maine

FY 71 (cont'd)
Grand Rapids, Mich.
Greenville, Mass.
Sikeston, Mo.
Portland, Ore.
Philadelphia, Pa.
Charleston, S.C.
Memphis, Tenn.
Richmond, Va.
Cheyenne, Wyo.

FY 72
Baltimore, Md.
Gadsden, Ala.
Hartford, Conn.
Macon, Ga.
Newport News, Va.

FY 73
Des Moines, Iowa
Fitchburg, Mass.
Lake Charles, La.
Pittsburgh, Pa.
Reading, Pa.

FY 74
Evansville, Ind.
Greenville, S.C.
Pittsfield, Mass.
Tacoma, Wash.
Washington, D. C.

FY 75
San Francisco, Ca.
Pine Bluff, Ark.
Gary, Ind.
Durham, N.C.
Springfield, Ill.

that site 4 years after the original sampling to take trend data. For cropland sites, in addition to a soil sample, a crop sample is collected when available. The following information is also obtained from the farmer:

- The crops grown on the site in addition to those sampled
- Irrigation used, if any
- The number of inches of irrigation
- Pesticides used
- Crop the pesticide was used on
- Formulation that was applied
- Pounds of active ingredient applied
- Method of application

After the sample has been collected in the field, it is sent to our central receiving laboratory at the Mississippi Test Facility. Here the samples are analyzed using primarily gas liquid chromatography. There is also a wide range of confirmatory instruments available for use, including atomic absorption spectrophotometry, liquid chromatography, and mass spectrometry. I'll go into more detail about the laboratory itself shortly.

After the chemical analyses have been completed, the resulting data are returned to the branch headquarters in Washington where they are statistically analyzed using either small desk-top computers such as the Hewlett Packard, 9100-B, or larger computer support programs. Presently all five of our monitoring programs are computerized.

The National Estuarine Monitoring Program

The objective of the National Estuarine Monitoring Program is to determine pesticide levels in fish in estuaries. Approximately 113 estuaries are sampled for two trophic levels of fish: herbivorous and carnivorous. Collections are made twice a year. Sampling teams attempt to collect only young of the year, since this age group indicates the current contamination load in the estuary. The samples are shipped to the Pesticide Monitoring Laboratory at Bay St. Louis, Mississippi for analysis.

Originally, this program sampled crustaceans and shellfish, which are good indicators of recent contamination. They are, however, able to purge themselves of residues within a fairly short period of time. Since insufficient resources were available to continue the program of monthly collections of shellfish, the program was redesigned in FY 1972. Fin fish were selected since they retain pesticide residues longer, are mobile, and are therefore a better overall indicator and integrator of pesticide pollution in an estuary.

The National Human Tissue Monitoring Program

The purpose of the Human Monitoring Program is to determine, on a national scale, the incidence and level of exposure to pesticides experienced by the general population and to identify changes and trends in these parameters when they occur. Pesticide residues and their metabolites that are detected reflect man's total exposure to these chemicals and his physiologic ability to handle them. This program was initiated in 1967 by the Pesticides Programs, Communicable Disease Center of the Public Health Service, and was transferred to the Environmental Protection Agency upon its creation in 1970.

The major thrust of the program is the collection and chemical analysis of samples of human adipose tissue. These are obtained through cooperating pathologists in 75 collection sites selected according to an experimental design in the conterminous 48 states (Figures 2 and 3).

Figure 2

National Human Monitoring Program
Collection Sites by State
FY 1975

- Alabama (6)
  - Mobile
  - Tuscaloosa

- Arizona (8)
  - Phoenix

- California (9)
  - Bakersfield
  - Glendale
  - Lakewood
  - Long Beach
  - Los Angeles - 2
  - National City
  - San Francisco

- Colorado (8)
  - Denver

- District of Columbia (5)

- Florida (5)
  - Hialeah
  - Panama City
  - Tampa

- Illinois (3)
  - Chicago - 3
  - Oak Park

- Indiana (3)
  - Evansville
  - Indianapolis

- Iowa (4)
  - Iowa City

- Kansas (4)
  - Salina
  - Wichita

- Kentucky (6)
  - Louisville

- Louisiana (7)
  - New Orleans

- Maryland (5)
  - Baltimore

- Massachusetts (1)
  - Boston
  - Pittsfield
  - Westfield
  - Worcester

- Michigan (3)
  - Bay City
  - Detroit
  - Wyandotte

- Minnesota (4)
  - St. Louis Park

- Missouri (4)
  - St Louis

- Nebraska (4)
  - Omaha

- New Jersey (2)
  - Hoboken

- New York (2)
  - Buffalo
  - Jamestown
  - New York City - 7
  - Troy

- North Carolina (5)
  - Charlotte
  - Winston-Salem

- Ohio (3)
  - Cleveland
  - Columbus
  - Mansfield
  - Parma
  - Toledo

- Oklahoma (7)
  - Enid
  - Oklahoma City

- Oregon (9)
  - Eugene

- Pennsylvania (2)
  - Erie
  - Hazelton
  - Philadelphia

- South Carolina (5)
  - Anderson
  - Greenville

- Tennessee (6)
  - Kingsport
  - Memphis

- Texas (7)
  - Dallas
  - El Paso
  - Houston
  - San Antonio

- Utah (8)
  - Salt Lake City

- Virginia (5)
  - Norfolk
  - Petersburg

- Washington (9)
  - Tacoma

- Wisconsin (3)
  - Beloit

Figure 3

Chemicals Detectable in the National Human Monitoring Program Multi-Residue Analysis of Adipose Tissue

Chemical	Limit of Detectability in PPB
o,p'-DDE	20
p,p'-DDE	10
o,p'-DDT	20
p,p'-DDT	20
p,p'-DDD	20
α -HCH	10
β -HCH	20
γ -HCH (lindane)	10
δ -HCH	10
Aldrin	10
Heptachlor	10
Heptachlor epoxide	10
Dieldrin	10
Endrin	20
Mirex	100
Oxychlordane	20
Trans nonachlor	NA*
Polychlorinated biphenyl	800
Hexachlorobenzene	4

*Not available at this time

A proportionate stratified sampling design is followed for selection of cities from which samples are collected. The number of cities needed in each census division is determined based on the total population in that division. This type of design provides data which are representative of the general population. For each collection site, an annual sample quota reflective of the demographic distribution of that particular census division is established.

Adipose tissue collected by cooperating pathologists is from postmortem examinations and from specimens previously removed during therapeutic surgery. Information recorded for each tissue sample analyzed includes age, sex, race, height, weight, pathological diagnosis, occupation, and geographic residence. Since the objective of the program is to reflect the pesticide burden in the general population, samples are not collected from victims of known or suspected pesticide poisonings, from chronically ill patients, or from patients institutionalized for extended periods.

All analyses are conducted by contract laboratories using only methodologies specified by the program. These laboratories are equipped with gas-liquid chromatographs with electron capture and other detectors. They are required to maintain acceptable performance levels in the Interlaboratory Quality Assurance Program moderated by EPA's Pesticides and Toxic Substances Effects Laboratory. This laboratory also provides technical consultation for the analytical portions of the program. All samples are analyzed for selected chlorinated hydrocarbon insecticides and polychlorinated biphenyls using a multiresidue approach. This procedure is capable of detecting metabolites as well.

Other human substances such as urine, blood, and milk are collected for analysis to detect some of the newer classes of pesticides. Currently a special project measuring organophosphate insecticide metabolites in urine is underway. I'll discuss that further in a moment.

The National Water Monitoring Program

A National Monitoring Plan for monitoring pesticide residues in fresh water was published in the June issue of the 1971 Pesticide Monitoring Journal. This plan had never been implemented. However, a cooperative program was eventually worked out between the U. S. Geological Survey and the Environmental Protection Agency, which was initiated in the fall of 1973. The Geological Survey collected the water samples at 132 sampling sites in 17 major river basins. We conducted the chemical analyses. Originally the design called for four water samples and two sediment samples to be collected each year from each station. However, only one paired collection of sediment and water was made in the first year of sampling. In FY 1975, all planned collections will be undertaken.

The National Air Monitoring Program

When one considers pollution in air, pesticides do not usually come to mind as being the primary pollutant. However, in certain situations such as during the height of the spray season in the Wenatchee Valley, pesticides in air can be a serious problem.

The National Monitoring Program for Pesticides in Air, which was in existence from 1970 through 1972, detected low levels of a large number of residues.

The sampling device which was used in that program was an impinger system. Basically, with that system, an air stream was bubbled through an ethylene glycol solution and the pesticides contained in that air stream were partitioned into the ethylene glycol. Under consideration for the future air program is a high volume air sampler. The advantage of the high volume air sampler over the impinger sampler is that it is a simpler machine, easier to operate, and it samples a larger volume of air to impinge pesticides onto a substrate. Therefore, the analytical sensitivity required to support this air sampling device is much less. In order to determine the best method of sampling air, both these instruments are currently undergoing extensive field evaluation. Upon completion of this study, the national air program will be redesigned and reinstituted.

The Ocean Monitoring Program

The oceans are generally considered an important sink for many persistent pollutants, and to date there has been no systematic monitoring of the oceans for pesticide residues on a continuing basis. The National Marine Fisheries Service approached us, suggesting that a cooperative program might be established between their organization and the Environmental Protection Agency. Basically, they agreed to supply ship time and collect fish samples at sea; our Agency would then do the chemical analyses and supply other monitoring support. Knowing that the Agency could not afford to pay the cost of ship time, we took advantage of this situation. In FY 1974, fish samples were collected on six ocean cruises on both coasts of the United States. The program at this time is viewed strictly as a pilot program. Its effectiveness will be evaluated and further decisions will be made as to whether it should be continued and possibly expanded.

Feed Monitoring

As mentioned earlier, the Food and Drug Administration is responsible for monitoring feed. However, after the episode with dieldrin contamination of chickens this spring, we were approached by Dr. Axelrod who suggested that a comprehensive pesticide monitoring program be established for animal feed and feed components. When FDA was contacted by Ecological Monitoring Branch representatives, they proposed an expanded cooperative feed monitoring program between FDA and EPA. This has been agreed to in principle by both agencies; negotiation of the actual details is still ongoing. Very tentative plans are for the collection of 750 samples in FY 1975, with an increase to 1,000 in FY 76; these samples would be analyzed at our MTF Monitoring Laboratory.

MTF Pesticide Monitoring Laboratory

This is an appropriate point to make additional mention of the Pesticides Monitoring Laboratory located near Bay St. Louis, Mississippi at the old NASA Mississippi Test Facility. At this modern laboratory of ours, there are an additional 24 persons including 10 chemists who provide the chemical support for the soil, water, and estuarine system, as well as for the various Special Ecological Projects. This amounts to an incoming sample load of about 6,000 samples per year and well over 12,000 analyses. Most samples are routinely analyzed for chlorinated hydrocarbon and organophosphate pesticides including the following. I'll try to add trade names where they may be helpful (Figure 4). For cropland soil, arsenic and triazine analyses are also conducted. Heavy metal analyses for lead, cadmium, arsenic, and mercury are being run or will be performed on estuarine samples and urban soil samples.

In the future we hope to add a multiresidue method for carbamates. Such a method is now under investigation and development by our supporting research laboratory.

Figure 4

Compounds Routinely Monitored for Organochlorine Compounds

Alachlor (Lasso^{T})
Aldrin
Benzene Hexachloride
Captan
Chlordane
Chlordecone (Kepone^{T})
Chlorinated Phenoxy Esters
Chlorobenzilate (Acaraben^{T})
DCPA (Dacthal^{T})
DDT's (o,p'-DDT; p,p'-DDT' o,p'-DDE; p,p'-DDE; p,p'-TDE
Dicofol (Kelthane^{T})
Dieldrin
Dithianon (Dicarbonitrile)
DMC
Endosulfan I (Thiodan^{T})
Endosulfan II
Endosulfan Sulfate
Endrin
Endrin Aldehyde
Endrin Ketone
Heptachlor
Heptachlor Epoxide
Isobenzan (Telodrin^{T})
Lindane
Methoxychlor
Mirex
Ovex
PCB's (Polychlorinated Biphenyls)
PCNB (Pentachloronitrobenzene)
Propachlor (Ramrod^{T})
Terpene Polychlorinates (Strobane^{T})
Toxaphene
Trifluralin (Treflan^{T})

Organophosphorous Compounds

Azinophosmethyl (Guthion^{T})
Carbophenothion (Trithion^{T})
Chlorpyrifos (Dursban^{T})
DEF (Degreen^{T})
Demeton (Systox^{T})
Diazinon
Dioxathion (Delnav^{T})
Disulfoton (Di-syston^{T})
Dyfonate
EPN^{T}
Ethion
Ethyl Parathion
Folex^{T})
Malathion
Methyl Demeton (Meta-systox^{T})
Methyl Parathion
Phorate (Trimet^{T})
Ronnel (Korlan^{T})

The recent addition of automated gas chromatograph injection equipment should allow the laboratory to increase its production. We are currently in the process of getting this equipment geared into our routine production.

Special Ecological Projects

In addition to the ongoing ambient monitoring networks, we also conduct studies we refer to as Special Ecological Projects. In the past, these were short-term monitoring studies on particular residue problems, initiated as a result of regular monitoring operations or at the request of another office within the Office of Pesticide Programs.

A study of the herbicide propanil and its metabolites in rice and rice soils exemplifies this type of effort. The metabolite TCAB has a similar chemical structure to that of a carcinogen and has been detected in rice soil as a result of normal use of propanil. This metabolite, an azobenzene compound, had been shown to form in laboratory tests in soil, but had never been detected from actual field usage. All samples have been collected for this project and they are awaiting chemical analysis at MTF. This study was initiated at the request of the Criteria and Evaluation Division.

Another special project is the study of the incidence and levels of organophosphate insecticide metabolites in human urine after a mosquito control application. Before and after aerial spraying in Dover, Delaware, urine samples were taken from people residing both in the target area and in a peripheral area. These samples are presently being analyzed. This type of human monitoring is of special public health interest, since the population of treated areas is unavoidably and directly exposed to the insecticides.

One proposed study for the spring of 1975 is a cooperative irrigation study with the Bureau of Reclamation, which is responsible for providing Federal aid to irrigation systems. This study would address problems associated with the fate and movement of pesticides in irrigation water and should provide valuable data for both agencies. The design of the study has not quite been initiated, but samples of water, sediment, soil, crops, and fish will probably be collected. This project will also impact on EPA's new water legislation as certain large irrigated areas are considered point-source polluters in terms of pesticides.

Our staff members were primarily responsible for the design and subsequent coordination of the collection of samples for the several phases of EPA's dioxin monitoring effort during FY 1974. In addition, the MTF Pesticides Monitoring Laboratory ran the extractions of the samples for this project. Branch personnel were also involved in evaluating the Forest Service's monitoring program for the DDT spray project against the Douglas-Fir Tussock Moth in the Pacific Northwest.

In the past year, the definition and scope of our special projects capability has been expanded to encompass more situations requiring pesticide monitoring expertise. Our appraisal of present and future monitoring requirements indicates that a continuing and increasing demand will be made of the capacities of our current networks and our special projects. With changes in pesticide technology and use patterns, our monitoring program will be shaped to continue to be responsive to Agency needs. In the future we anticipate that monitoring activities will extend into the following areas.

1. Experimental Permits — The responsibility for monitoring experimental permits is usually placed upon the industry or organization making the application. However, in certain cases, the Agency may find it to its advantage to conduct monitoring activities either in addition to or in cooperation with the organization seeking the permit.

2. Emergency Pesticide Use — Monitoring programs would be involved with requests to the Agency for the use of pesticides on an emergency basis under

section 18 of the amended law. We would provide technical surveillance over such applications in terms of ecological effects.

3. Classification and Reclassification of Pesticides — Data from both our continuing surveillance system and special short-term projects will be used in the classification and reclassification of pesticides as required by the amended law.

4. Litigation Proceedings — Monitoring information from our established networks and from special studies continue to be useful for fact-finding, cancellation, and suspension public hearings.

5. Alternative Chemicals Program — Planning for monitoring input into this Agency program has been underway since its creation. The monitoring requirements of this program will be varied.

6. Operational Surveillance — Surveillance monitoring does not fall into the classic definition of pesticide monitoring; it is an area in which we have only recently become involved. It centers around the development of methods and plans to oversee special pesticide applications to ensure that these conform to Agency requirements and environmental impact statements.

Use of Data

Yearly summaries of all the programs and most special projects are published in the open literature and in internal reports by EPA. The data generated by our numerous monitoring projects is actively utilized in the Agency and by others. Data have been requested by parties on both sides for use in the ongoing pesticide litigations on mirex, aldrin, dieldrin, and mercury. Our personnel have testified as expert witnesses in several fact-finding, cancellation, and suspension public hearings.

In addition, requests for data are received from universities, chemical companies, and offices of state and Federal government. Since last January, nearly 300 written reprint requests have been received, mostly from state governments. A considerable number of inquiries for information and advice are handled by our personnel.

Most of our findings have dealt with residue levels in various media. Now that the programs have been conducted for several years, we will be examining the data to detect changes and trends in pesticide use and residue levels. Also, the addition of graphic support should aid in conducting and displaying results of these comparisons. All comparisons will, of course, have to be statistically based, but visual displays should be particularly helpful to a variety of users of our data.

The five EPA National Pesticide Programs and those of other agencies need to have the data from their systems integrated to determine what relationships exist. The feasibility of such a project is now under investigation in our Agency as an independent review, and a final report will be completed this winter.

DR. R. R. WHETSTONE: You have discussed monitoring pestidice residues. Will the program include monitoring of phenomenon rather than pesticides, such as photosynthesis in the ocean?

DR. WILLIAM MURRAY: I would like to believe that this lies just ahead. Certainly we're in the process of making the transition from monitoring residues to monitoring residues and determining what they mean, in other words, effects monitoring. I think what you're referring to is just around the corner. It is going to require some additional expertise on our staff and some additional support, but this is certainly very important to us.

QUESTION: There are two questions I'd like to ask. One, have you noticed any change in trends in amounts of DDT in humans since it's been phased out, and if not is that to be analyzed as a part of your program? And second, in the case of the propanil are you taking both plant samples and soil samples from the same sites?

DR. MURRAY: The latter answer is yes from both sites. The former question is a little bit more difficult, and there's an opportunity to get into trouble here in oversimplifying. Nevertheless there has been a small drop in the amounts of DDT in the average person's body. The reason I'm being a little careful here is because it depends on a number of factors including geographic location and some other demographic parameters, i.e., age, sex, race. So the answer is really quite complicated, and I'm not prepared to give it in any more detail.

MR. TOM BLUE: With respect to the soil monitoring program and the collection of data from the farmers as to the types of pesticides used and so forth, over what time frame do you collect these use data and relate them to what's in the soil sample? And do you analyze for all of the chemicals applied over that time period?

DR. MURRAY: The soil monitoring program has been going on for 5 years. To answer your last question, I did read, very briefly of course, the kinds and numbers of pesticides for which we analyze the soil samples.

PESTICIDE RESEARCH
IN THE U.S. DEPARTMENT OF THE INTERIOR

Jerry R. Longcore*

I appreciate the opportunity to attend this Symposium on the Alternative Chemicals Program and to participate in this overview of pesticide research. In the following, I will present a brief resume of the various agencies of the Department of the Interior that are engaged in pesticide studies.

The Department's efforts in pesticide research are primarily concerned with two areas: (1) to evaluate pesticides in the laboratory and the field for their toxicity, sublethal effects, and hazards from specific uses to fish, wildlife, and the environment and (2) to gather data required for registration of specific chemicals — chemicals that are necessary to meet the responsibilities of many of the land management agencies of the Department.

First, I would like to discuss the pesticide efforts in the Fish and Wildlife Service and then touch upon the efforts in other agencies of the Department.

Fish and Wildlife Service

Department research efforts in the above mentioned areas are carried out primarily in the Fish and Wildlife Service, which, in addition to pesticide research per se, has the responsibility for animal and bird damage control and thus needs suitable control agents (chemical or otherwise). Wildlife damage to agricultural crops in some geographical areas is extensive; fruit and cereal crops are especially affected. A number of compounds are utilized in the Federal Fish Hatchery Program, and many other Service agencies need chemicals for vegetation control or other pest control problems. Under the Fish and Wildlife Act of 1956, the Service also has the responsibility of investigating the effects of polluting substances on fish and wildlife.

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Because many of the Department's chemical needs are in the so-called minor-use category (i.e., expected use too small to interest industry in registering a chemical for a particular use), it must register chemicals through its own or cooperative efforts with other agencies or industry.

The main laboratories involved in pesticide research and the general thrust of the research are as follows:

FISH CONTROL LABORATORY La Crosse, Wisconsin	Registration of chemicals for fishery management. Evaluation of hazard of pesticides to fish and the aquatic environment.
SOUTHEASTERN FISH CONTROL LABORATORY Warm Springs, Georgia	Registration of chemicals for fishery management.
GREAT LAKES FISHERY LABORATORY Ann Arbor, Michigan	Determination of pesticides in Great Lakes fish. Evaluation of the effects of pesticides in fish.
SOUTHEASTERN FISH CULTURAL LABORATORY Marion, Alabama	Evaluation of hazards of pesticides in aquatic environments.
FISH-PESTICIDE RESEARCH LABORATORY Columbia, Missouri	Evaluation of hazards of pesticides in aquatic environments. Registration of chemicals for management (primarily herbicides).
DENVER WILDLIFE RESEARCH CENTER Denver, Colorado	Evaluation of hazards of pesticides to wildlife. Registration of animal damage control chemicals. Registration of bird damage control chemicals.
PATUXENT WILDLIFE RESEARCH CENTER Laurel, Maryland	Evaluation of hazards of pesticides to wildlife. Registration of bird damage control chemicals.

While laboratories collect data for registration, they also obtain information on hazards related to the use patterns for which the registration is sought. However, the Wildlife Research Centers at Denver and Laurel and the Fish-Pesticide Laboratory at Columbia do most of the studies of the effects of pesticides on non-target organisms and the environment. In addition to the laboratories mentioned, 20 Cooperative Wildlife Research Units and 25 Cooperative Fishery Research Units are located at 26 universities and supported by the universities, the state agencies, and the Fish and Wildlife Service. A limited number of pesticide studies are conducted at these research units.

The above has covered the why and the where of the pesticide research in the Fish and Wildlife Service. The question of what is being done can best be depicted by examples of the two major research thrusts, registration and ecological evaluation of effects on non-target species.

Registration of Chemicals

Efforts related to obtaining registration data encompass a variety of studies. These investigations include but are not limited to toxicology, chemistry, efficacy, uptake and elimination, degradation and identification of metabolites, and residues.

Examples of chemicals now under study for use in fishery management include TFM (3-trifluormethyl-4-nitrophenol) with Bayer 73 (2'5-dichloro-4'-nitrosalicylanilide), a lamprey larvicide; antimycin (an antibiotic substance produced by Streptomyces spp.), a fish toxicant; certain herbicides (simazine, diuron, endothall, and diquat); and Thanite (terpinyl thiocyanoacetate), dylox, and a number of other compounds, including some used as drugs or therapeutics.

Current efforts in the registration of animal control chemicals include work on zinc phosphide for control of prairie dogs on rangeland, jack rabbits (agricultural crops), pocket gophers (crops and forests), voles (agricultural crops), ground squirrels (rangeland), and rats (sugarcane); Mestranol, which is used as a repellent for white-footed mice in forestry management; and medroxyprogesterone acetate (a reproductive inhibitor), which is needed for deer control in certain park areas.

Compounds being studied to alleviate bird damage include avitrol for blackbird control in sunflowers, sweet corn, sorghum, and field corn; and methiocarb for blackbird control in sprouting field corn, rice, and wheat and for control of bird damage in cherries, blueberries, and grapes. Certain wetting agents are being evaluated for population reduction of blackbirds at undesirable roost sites. In an attempt to discover species differences that may be exploited for control purposes, chemical metabolism by liver microsomes is being studied in the red-winged blackbird.

Evaluation of Pesticide Hazard

Our evaluations of pesticide hazard to non-target species are based on broad ecological field investigations supported by controlled laboratory experimentation. Included in these studies are certain standard bioassays or tests of acute toxicity. Current and continuing ecological investigations of wildlife include studies of problem chemicals in sensitive and/or especially exposed species such as black-crowned night herons, other herons, brown pelicans and associated seabirds, bald eagles, ospreys, bats and insectivorous birds, and waterfowl. Ecological studies also include evaluation of specific uses of certain chemicals such as toxaphene on rangeland, endrin on pine seeds, and aldrin and furadan in rice culture.

Laboratory experimentation on the effects of pesticides on reproduction, behavior, enzyme systems, and on pesticide kinetics (accumulation and loss) and lethal residue levels are conducted with a number of avian species: mallards, black ducks, bald eagles, kestrels, bobwhite quail, coturnix quail, pheasants, starlings, red-winged blackbirds, cowbirds, grackels, ringed doves, and homing pigeons. Experimental colonies of barn owls and black-crowned night herons will be ready for pesticide studies this coming year.

The following selected research highlights may give an indication of the variety of studies and elucidate the scope of this pesticide research. These examples of research findings are typical of work being done at the Patuxent and Denver laboratories.

Kelthane, an organochlorine acaricide structurally similar to DDT, increased mallard embryo mortality when females were fed a diet containing low levels of the pesticide. Mercury (methylmercury) was found to adversely affect reproduction of mallards, black ducks, and ring-necked pheasants; it has been found to be highly persistent in duck tissues, but after the moult the body residues drop conspicuously. Aroclor 1242, when fed in the diet, caused a thinning of coturnix quail egg shells.

New pollutants have appeared in bird tissues; octachlorostyrene and related isomers have been identified from a bird sample, and hexachlorobenzene (HCB's) is occurring in bird and fish species.

Studies of bald eagles found dead in the field have revealed that enough dieldrin has accumulated in the brain of some individuals to cause death.

Studies of DDE in free-tailed bats indicate that young bats obtain much of their DDE via the nursing female's milk. Mortality of young free-tailed bats reposed in a Texas cave was shown to have been from starvation and not from pesticide poisoning.

Oxychlordane (a metabolite of chlordane), when tested in several species of blackbirds, was nearly as toxic as dieldrin; it was accumulative and persisted in the tissues.

Parathion, when fed to quail after they had been fed methylmercury, was found to be more toxic than when used alone. This indicates the potential problem of multiexposure of organisms to pesticides and other pollutants.

Multienzyme analysis has shown toxicant-specific responses to ingested chemicals, and for some enzymes, dose-related responses. Enzymes were studied in starlings and the chemicals Morsodren, DDE, Aroclor 1254, and malathion were evaluated.

Our research on pesticides in aquatic organisms, which is carried out primarily at the Fish-Pesticide Laboratory and its field stations, is done on those chemicals that meet the following criteria:

1. Pesticides (or other chemicals) that have established uses, either terrestrial or aquatic, which are considered to be aquatic contaminants already in the environment.

2. Pesticides that are being considered for aquatic use in resource management. This research is often in the form of gathering data for registration.

3. Chemicals that are being commercially registered for uses with high potential for producing aquatic contamination. These are frequently new chemicals or new uses of existing chemicals that are being developed for commercial application.

The goal of the research is to unravel the obscure and subtle overall effects of pesticides on aquatic ecosystems. To do this requires a multidisciplinary approach involving a team of scientists. The scope of the work encompasses the following:

1. Acute and chronic toxicity of pesticides to fish and aquatic organisms.

2. Influence of environmental factors on toxicity.

3. Bioaccumulation and biotransfers of pesticides in segments of the aquatic food web.

4. Toxic interaction of pesticides.

5. Pesticide-induced pathology in fish.

6. Effects on metabolism, growth, behavior, nutritional state, and hormonal response of fish.

7. Influence of pesticides on hatching success of fish.

8. Determination of enzymatic modes of action of pesticides.

9. Pesticide behavior in water, mud, fish-food organisms, and fish.

10. Development of analytical methods for pesticides and associated industrial pollutants.

The following research highlights on this aspect of the work may serve as examples to further illustrate the varieties of the research performed:

Guthion and leptophos were the most toxic of a group of 32 pesticides tested on freshwater fish. A dinitrophenol herbicide, dinoseb, was more toxic (10-100 ug/1) than most herbicides.

Toxaphene at 10 to 32 ug/1 delayed midge emergence and appeared to inhibit mating.

Changes in alkalinity of pH 7.5 to 9 increased the toxicity of some pesticides substantially; for example, zectran toxicity increased 25-fold.

Endothall accumulation was below detectable limits (20 ng/g) in rainbow trout at 1 or 12 hours after application at practical rates to an artificial stream.

Hepatic microsomal preparations from channel catfish metabolized di-n-butyl phthalate to phthalic, palmitic, oleic, and stearic acids, which were identified by GC-MS and radiolabeled standards on TLC.

The highest organochlorine residues in eggs from striped bass collected from females in spawning migration from the East coast were 10-fold those which have been causing problems in salmon in Sweden.

As mentioned above, some research on non-target species is being done at the Great Lakes Fishery Laboratory. Studies here include surveys of mercury, the DDT complex, dieldrin, and PCB residues in the Lake Michigan fish; a survey of lead in fish of the Great Lakes; effects of PCB's on uptake and storage of DDT and DDE from water by the lake trout; baseline measurement of the enzyme allantoinase in Great Lakes trout; and determination of the subcellular binding or storage sites of contaminants in the lake trout.

About 10 of the Cooperative Wildlife Research Units and 5 of the Cooperative Fishery Research Units are evaluating the hazards to fish of dieldrin, PCB's, DDT, and mercury.

Through the Federal Aid in Wildlife Restoration Act and the Federal Aid in Fish Restoration Act, certain monies are made available to the states for related fish and wildlife restoration projects. A number of states have utilized these funds to conduct pesticide residue surveys or limited research on pesticides and other pollutants. For example, the California Department of Fish and Game is investigating the effects of certain herbicides on a big game habitat supported by a Federal aid project.

Other agencies of the Department of the Interior that conduct or support pesticide research include the Bureau of Reclamation, Office of Water Research and Technology, and the National Park Service.

Bureau of Reclamation

The Bureau of Reclamation has been involved for some time in research on pesticides for the control of aquatic and ditchbank weeds and other pests in irrigation systems. Early studies centered on finding effective methods of controlling plant pests. New studies are concentrated on obtaining the information necessary to register pesticides that are useful and safe. The Bureau is continuing with research projects aimed at finding better pest control methods and evaluating habitats produced by irrigation systems.

Bureau of Reclamation projects provide about 20 percent of the irrigation in the Western United States. The pest control methods and the pesticides developed and registered by Reclamation are used, not only in its own operations, but by water user organizations that operate many of the Bureau's projects and also by a number of private irrigation developments.

A considerable amount of information is necessary to register pesticides for use on irrigation water distribution and drainage systems. Residue data are needed for drinking water, agricultural crops, and fish and animals that may drink the water or eat the irrigated crops. Because pesticide uses are in the minor-use category, Reclamation must underwrite or share the cost of registration with other agencies.

The Bureau's main research facilities are located in the Engineering and Research Center in Denver, Colorado. The center is fully capable of analyzing for pesticide residues. Research is conducted in cooperation with the Fish and Wildlife Service and the Agricultural Research Service. The Bureau of Reclamation usually determines residues in water; the Fish Pesticide Research Laboratory of the Fish and Wildlife Service obtains residues in fish; and the Agricultural Research Service obtains residues in crops.

Field studies are conducted on Reclamation projects at various field locations which allow for collecting samples under varied field conditions.

The Bureau also has limited funds for research through their regional offices. Studies are being conducted by the University of California at Davis in cooperation with the Agricultural Research Service and state agencies. One project is to evaluate the white amur as a method for weed control.

The Bureau of Reclamation is cooperating with the Fish and Wildlife Service on studies of zinc phosphide for control of meadow mice and ground squirrels.

Reclamation works closely with agricultural chemical companies to obtain product registration either by conducting research that yields data that the companies use for registration or by identifying informational needs relative to registration.

The Bureau of Reclamation encourages studies through cooperative agreements with the Environmental Protection Agency and other agencies, because the registrations they obtain often have utility for many other Federal and non-Federal agencies.

Office of Water Research and Technology

The Office of Water Research and Technology in the Department of the Interior supports about 330 contract studies on water quality management and protection. A number of these involve pesticide and other pollutants in aquatic environments as related to water quality. The 1973 Water Resource Research Catalog, volume 8, parts I and II, gives details of these currently supported research contracts.

National Park Service

The National Park Service has a preliminary study dealing with arsenic accumulation in a species of stone crab, which is being done at the National Park Service's Science Center located at the NSA/Mississippi Test Facility in Bay St. Louis, Mississippi.

FROM INDUSTRIAL R & D TO THE MARKETPLACE

Edwin F. Alder, Ph.D.*

It is a pleasure to be with you this afternoon representing the National Agricultural Chemicals Association. We are pleased to be able to include the view of industry in this overview of worldwide pesticide research.

It seems appropriate that this pesticide symposium should be held here in Denver where the first housewives' supermarket revolt over higher food prices was staged several months ago — appropriate because our subject, pesticides and their usage, has been a big factor in helping to keep expenditures for food in the United States down to a lower percentage of total income than that in any other major country in the world. But, as Professor Kljajic and others have pointed out today, the worldwide demand for food is increasing. Even in this country, low food prices and the luxury of surpluses appear at an end. And it will require the best scientific efforts of industry, government, and the academic world to meet the demands of the future.

Research and Development of a Pesticide

The purpose of my discussion today is not to justify pesticide usage, but to acquaint you with at least a part of the research and development that goes into a new pesticide, and to identify some of the major problems and issues facing continued development of new, effective, and environmentally compatible pesticides.

You have heard many times that it now takes $6 to 10 million and 7 to 10 years to find and develop a new pesticide. Let's see just what this expenditure of time and money gets for us as consumers.

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*Vice-President, Lilly Research Laboratories.

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The expenditure can best be summarized by the pesticide label. Each pesticide label gives the chemical name of the pesticide, identifies areas of use, and provides application directions along with certain precautions or restrictions. Behind the label is a huge research effort that has required the ingenuity and labor of dozens of scientists, specialized equipment and laboratories, and literally hundreds of tests to prove the efficacy and safety of the chemical in actual usage.

In its most elementary form, the development of a new pesticide can be said to center on two areas: efficacy and safety. Efficacy data demonstrate that the pesticide kills certain insects, controls certain plant diseases, or kills certain weeds. Safety data demonstrate that the pesticide is safe to the applicator, others exposed to the treatment, consumers of the products, the environment including wildlife, birds, and fish, and the crop to be treated.

The requirements which may be necessary for registering a new pesticide result in volumes of data. In the development of our company's major herbicide product, the research results contained in 110 notebooks have been collected and submitted to Federal government agencies during the past 11 years. The types of data that must be developed can be roughly categorized as biological, toxicological, environmental, and chemical with considerable overlapping and intermeshing of these categories.

Some of the biological parameters are shown in Figure 1. To have a pesticide, first we have to find biological activity. This we do by screening chemicals for the desired pesticidal activity. Once that is in hand we determine the rate range required for pest control. And we determine the method, the technique of application — will it be applied to the soil surface, the foliage, incorporated into the soil or how? Through further field studies we determine the spectrum of pest control, crop tolerance, chemical and physical compatibility of the compound when mixed with other pesticides likely to be used in the same application, the half-life in soil and animals, the rate and method of dissipation in the soil, the duration of biological activity (or the persistence), and the run-off and leaching characteristics. In addition, in these field studies we observe any effects on crops that follow in the crop rotation.

Figure 1

Biological

Screen for biological activity:

- Insecticide
- Fungicide
- Herbicide
- Growth regulator

Rate range studies for efficacious pest control

Application techniques:

- Soil incorporation
- Foliar
- Soil surface

Determine through field trials:

- Spectrum of pest control
- Crop tolerance
- Compatibility with other pesticides
- Half-life
- Soil dissipation
- Duration of biological activity
- Runoff and leaching
- Crop rotation practices

Manage experimental permit program

Provide technical service to the user

As development progresses we establish an experimental permit program and eventually, after the product is on the market, provide technical service to the user.

Figure 2 lists the types of toxicological data which may be required for the establishment of a pesticide tolerance in food crops. The general types of information are acute toxicity, subacute toxicity, and chronic toxicity along with special studies.

Figure 2

Toxicological

Acute toxicity:

- Oral LD_{50}
- Dermal LD_{50}
- Eye irritation
- Inhalation LC_{50}
- Skin irritation

Subacute toxicity:

- 90-day feeding
- 21-day dermal
- 21-day inhalation
- Skin sensitization

Chronic toxicity:

- Chronic feeding 2-year including carcinogenic evaluation
- Three generation reproduction
- Teratogenic
- Mutagenic

Special studies:

- Metabolism
- Antidote
- Neurotoxicity
- Gastrointestinal irritation
- Lung irritation
- Toxicity interaction

Acute toxicity studies include the obtaining of oral and dermal LD_{50} in mammals as well as eye irritation, inhalation, and skin irritation studies. Subacute toxicity includes a 90-day feeding study, 21-day dermal, 21-day inhalation, and skin sensitization. Chronic toxicity studies include the 2-year feeding study with a carcinogenic evaluation, 3-generation reproduction, teratogenic, and mutagenic studies. Special studies may include metabolism studies, search for an antidote, determination of neurotoxicity, gastrointestinal irritation, lung irritation, and any toxicity interaction discernible.

Figure 3 depicts the kinds of investigations carried out to determine the impact of pesticides and their degradation products on the environment. As previously mentioned, research is required to determine the rate of dissipation in the soil and the duration of the biological activity. The methods of degradation (such as decomposition by light and microorganisms or chemical degradation) are studied. Leaching studies determine the amount and rate of movement downward and laterally through the soil with water. The amount of chemical removed in surface run-off water must be determined, along with any adverse effects that the chemical may have. The release of soil-bound material by subsequently planted crops and the accumulation of the compound or its metabolites in fish, mammals, and birds are studied.

The chemists' contributions are listed in Figure 4. The outline program, of course, started with chemical synthesis and was followed by the preparation of related compounds and studies relating to structure and activity, and culminated in patent applications in various appropriate parts of the world. The chemical-physical properties had to be established. Analytical procedures had to be developed to find the chemical in plants, soils, and animals. It is the chemist we look to to determine the metabolites — the breakdown or decomposition products — and he must determine the rate of breakdown in the soil or in the crop. The stability of the product in the container must be evaluated to ensure that the product remains usable for the length of time it is likely to remain in storage. Various chemical manufacturing processes must be studied, with considerable attention given to the process which uses the least expensive, most readily available raw materials and which produces the most environmentally compatible waste streams. The cost of production must be determined and procedures eventually set up to monitor and maintain control of the quality of the chemical.

Figure 3

Environmental

Rate of dissipation in soil

Mechanism of degradation:

- Photodecomposition in soil and water
- Effect on microorganisms
- Effect by microorganisms
- Degradation in water
- Duration of the biological activity

Leaching studies

Runoff studies

Release of soil-bound material by subsequent plants

Accumulation of products in fish, rabbit, and bird tissue

Only a part of the research required to establish the efficacy and safety of a pesticide has been shown. New and improved techniques are constantly being developed and will be used as soon as their dependability and relationship to the real problems under study are established.

The comment was made yesterday that many of the current pesticides were registered 10 to 25 years ago when requirements were much less stringent. This is true, but for many of the major products, new indications of use and new label claims have, in essence, caused the compound to be reregistered many times over the years. At each label revision new research information has been submitted. Thus, we have kept up an ever-improving technology base.

Figure 4

Chemical

Chemical synthesis

Analog synthesis

Chemical structure-activity studies

Patent preparation and submission

Determine/develop:

- Chemical-physical properties
- Analytical procedures for plants, soils, and animals
- Biochemistry metabolite research
- Decline curves for soil and crop
- Different formulations — E. C., W. S., W. P. granules
- Stability of different formulations
- Chemical manufacturing processes
- Cost of manufacturing data
- Chemical quality control measures

Status and Outlook of Pesticide Industry R & D

What is the current status of industry research and development effort, the health and outlook of the pesticide industry? In 1970, there was an industry profile study carried out by NAC. A questionnaire was sent to companies conducting pesticide research and development. Thirty-three of these companies responded to a private accounting firm that assembled the data and attempted to draw an industry profile.

A few results from that study are shown in Figure 5. The 33 participating companies reported $69.9 million in pesticide research and development expenditures in 1970 — an increase of 33 percent over 1967 expenditures, though much of this increase was thought to be not research on new compounds but research to maintain present products on the market.

Figure 5

Pesticide R&D Expenditures of Participating Companies

	1967	1970	% Increase 1967-70
R&D Expense ($ Millions)	52.4	69.9	33

Figure 6 gives some measures of the time and effort required to develop pesticides. These figures indicate that the surveyed firms applied 2,768 man-years to pesticide R & D activities in 1970. One might view this as a measurement that excludes the effects of inflation and simply sums up the human effort applied.

Figure 6

Measures of R&D Activity in Participating Companies

	1967	1970	% Increase 1967-70
Man-Years expended	2368	2768	17
Dollar expenditures ($Millions)	52.4	69.9	33

Another consideration (Figure 7) was the time required from pesticide discovery to marketing and use. This was growing rapidly. The cost of discovery and development of a marketable pesticide product was estimated at $5.5 million in 1970 — up 60 percent from 1967. The combined opinion of surveyed companies was that about 77 months are required to take a compound from discovery to marketing — an increase of 28 percent in the time required since 1967. We suspect that these rates of increase since 1970 will prove to be linear.

Another similar study to update the 1970 report has just been carried out by NAC and will be available this fall. In addition, the EPA has commissioned a study to attempt to determine the effects of FIFRA amended on industry research and development. From these two surveys, we should be able soon to obtain a more up-to-date picture of the health of industrial research and development of pesticides.

Figure 7

Industry Estimates of Typical Pesticide Development Requirements

	1967	1970	% Increase 1967-70
Cost of discovery and development ($ Millions)	3.4	5.5	60
Elapsed time from discovery to marketing (Months)	60	77	28
Number of compounds screened for each new product marketed	5481	7430	36

You have heard from time to time of the companies that have dropped out of the pesticide business, or dropped segments of R & D activity, or reduced their overall scale of operations. Various reasons have been given for these actions, with excessive government regulation one of the more prominently featured reasons.

However, if you will examine carefully the companies that have gone out of the pesticide business, you will find that some of them were scarcely ever in it. They really didn't have the commitment to the kind of research and development effort that is required to put a pesticide on the market. Some thought it was a shortcut to profit and found out to their sorrow that a lot of patient money is required to develop and market pesticides. Other companies became discouraged when their present major products were in jeopardy for one reason or another. Or, in still other cases, the pesticide business represented a very small part of the company's overall business, and the company felt that it was contributing a bad image to their major activities and therefore elected to drop out. Whenever there has been substantial new technological activity in an industry — whether it be automobiles, electronics, aircraft, plastics, drugs, or whatever — there has been a shakeout of companies. Some shouldn't have been in the business in the first place, have recognized it, and have left. Others have fallen behind and withdrawn. Others have merged or sold out and disappeared from the scene. This is certainly not an abnormal situation or necessarily an unhealthy one. The pesticide industry is no different in this respect from other high technology industries. We'll have some Nashes, Hudsons, and Packards and even a few Edsels in the pesticide business.

But, as some of the companies have gone out of pesticide research in this country, other foreign companies have come in. We now have an array of German, Swiss, British, and probably eventually Japanese activities filling the gaps. We have not seen any lessening in competition in this business. The state of competition in pesticide research and development remains quite healthy.

Future of Pesticide Industry R & D

As to the future, up until now some of us have viewed the situation rather philosophically and simplistically and made some basic assumptions: That people are going to have to eat; to eat we are going to have to grow more food for more people; we are going to have to control pests; and the bulk of pest control must be done by the use of pesticides. To have pesticides we must have research. We must have research to maintain present pesticides on the market and to introduce new and better materials to control resistant pests or newly introduced pests around the world or to improve on the safety or environmental properties of older, less desirable products.

As agriculture has grown and continues to grow increasingly important in this country (as it has in the past 2 years when countless millions learned for the first time that groceries don't arise de novo in the grocery store) we have assumed that all inputs for agriculture will likewise become more important and that there is a place for industry in producing pesticides and in doing research to bring new products on the market and that this will continue to be the situation for many years to come.

We in industry are not pessimistic about the future of agriculture, the need for new technology in agriculture, or the contributions we can make to agriculture, to the welfare of our country, and to the welfare of mankind. We have felt that, over the long run, we are in a growth industry, one that is limited only by our own innovative capabilities.

Pesticide Industry Concerns

So what are our problems? What are we concerned about? We have a number of concerns, some growing and others diminishing in importance.

Perhaps the most serious threat to pesticide research over the past 2 decades may very well be certain new regulations now being promulgated. Some of us had rather naively thought that any regulatory hurdle put in our path could be overcome by research -- that as long as regulations were administered fairly, we could survive. Now we are not that convinced, primarily because our capability to do research is being challenged as never before.

A specific grave concern, which is now fading, was the proposed regulations on experimental use permits. These regulations as they were initially proposed would have unquestionably curtailed our research effort, caused our efficiency to decline, greatly increased the cost of doing research, and lengthened the time for any payoff on research investment. If these regulations had not been substantially modified, our research costs would have increased; research would have, in part, been encouraged to move out of the country; costs of pest control would have increased; and American agriculture and eventually the consumer would have been the poorer for it. We are pleased to report that the new draft of the regulations appears much more acceptable and we would urge its adoption.

Another concern is the recurring notion that the government or some "independent" contractor can do the job of researching and registering pesticides better, or at least more honestly, than private industry. I would submit that no individual really familiar with industrial research would challenge the integrity of the industrial scientists. I am proud of the integrity and responsibility shown by the scientists in my company and in the companies with which we compete. We as scientists are well aware that our data must be honest and must be scientifically sound. Our work must stand up in the scientific community as well as withstand the scrutiny of regulatory agencies, and it must stand the ultimate scrutiny, the crucible of the marketplace. Remember that industry scientists have received the same basic training as "independent" scientists, schooled in the same scientific philosophy and integrity, under the guidance of the same academic scientists. We didn't lose the principles instilled by such training just because we went to work for industry. Moreover, because of our motivation, we in the private sector feel we can discover and develop pesticides more efficiently than any other sector.

We have frequently heard that incentives should be offered to industry to develop new and better pesticides. What is industry's feeling on incentives? Frankly, some of us run for shelter or look for the nearest exit when any government group mentions providing incentives for us. By the time the "incentives" are brought forth, they usually turn into dis-incentives.

A good example of this is the compensation for use of data provision of FIFRA amended. This provision was, we are sure, intended to be an incentive for industry. It is proving to be a headache to many of us in industry as well as in government. For the record, we are, nevertheless, hopeful that the final regulations will prove equitable and workable.

As a genuine incentive we have constantly pleaded for faster reaction to registrations. We are confident that important steps are being made in this direction. Recent reorganization of the Pesticides Registration Division to institute a product manager system is indicative of EPA's interest in increasing efficiency in the registration process. We are hopeful that these product managers can work effectively between industry regulatory representatives and EPA reviewers to decrease the time required to get registrations.

We are always concerned in any review that recognition should be made that each individual use of each compound must be considered separately. Blanket condemnations and categorizations of compounds are not good science or good economics and are very poor politics. Persistence per se should not be equated with evil. Some compounds need to be persistent to be effective. Only by looking at each intended use of each compound along with its chemical and biological characteristics can sound judgments be made.

Another concern of industry is government grants for research studies. The unknown is always feared. When research grants on our established products are let and we read about them in the "Commerce Business Daily," we are naturally fearful. Why is this study being run? Were our submitted data inadequate? Are the contractors really familiar with the analytical or other techniques that we have struggled with for years? Does EPA know we have data on file that answer these questions? Why didn't they tell us? How can we find out what's going on? We would earnestly plead to be dealt in on the action. If there are questions, let us present the information we have. Perhaps data have been lost or misplaced. Any information EPA can provide us on the reasons for letting a grant will be most welcome. If a compound is not really suspect, any reassurance that can be offered will serve to strengthen our confidence in the regulatory process and to dispel our fears that some precipitous action is under way. Our request for more information is, we recognize, difficult to consistently put into practice. It would, however, appear to be in accord with the policy of openness in EPA which was expressed and reiterated yesterday.

Positive Aspects, Present and Potential

Well, what's going right? Actually, many of the concerns I have mentioned are diminishing as later draft regulations are forthcoming and better communications and mutual trust are established. Other positive things are happening.

The efforts of the Criteria and Evaluation Division of EPA to initiate studies through grants programs to develop new methodology to deal more effectively with the "genesis" questions are laudable. We urgently need new test methods to measure carcinogenic, teratogenic, and mutagenic potential. If we could determine which compounds will likely present problems, we could abandon them before we invest heavily in them, and we could then devote our resources to safer compounds and greatly improve our efficiency.

We would further plead that for genesis evaluations to be really meaningful they must relate to the use levels of the pesticide. We must get some concept of dosage response into these evaluations. Long-term dosage of high levels of pesticides to test animals does not represent actual exposure conditions in the environment or necessarily yield useful data. Such evaluations work to the severe disadvantage of compounds having low acute toxicities, when they are tested at unrealistically high levels simply because long-term high dosage studies are possible. As Dr. Coulston pointed out this morning, any time that we exceed the capacity of the test animal to metabolize a compound in a long-term study we are likely to encounter liver tumors late in its life cycle. Paradoxically, chemicals that are highly toxic in single doses and potentially more hazardous to the applicator may come into greater use because the acute risk, even though high, can be measured and the long-term risk cannot. We would, therefore, make the plea that the "maximum tolerated dose" be replaced by a dose level arrivod at by careful consideration of the test animal's metabolic capacity and the potential residues.

A cooperative field tour training program is now being established. This program, which has been enthusiastically supported by industry and EPA, is to permit field tour training in industrial settings for individuals in EPA who review applications for registration and who draft regulations and guidelines, and for other key personnel. This will better acquaint them with techniques and programs used by industry in the development of new pesticides and perhaps instill greater confidence in the quality of industrial research. We are optimistic that it will provide a greater understanding and appreciation of the roles of both industry and EPA.

There has been considerable discussion in EPA and elsewhere about the development of new pesticides and the maintenance of current pesticides cleared for minor crops or for minor uses. Increased requirements for registration and increased costs of doing pesticide research threaten the continued flow of new, safe, more effective pesticides for use on minor crops. We are pleased that a temporary coordinator for minor-use pesticides has been appointed. We suggest the following ways that industry can be encouraged to work on minor crops:

- Establish crop tolerances by commodity grouping.
- To avoid seizure liabilities, set tolerances for minor crops at toxicologically safe levels rather than the maximum encountered in tests.
- Accept data on performance and residues from selected major crops to represent minor crops insofar as possible.

We realize that some aspects of these suggestions may require new law or new regulations, but with these approaches we think the minor-crop problem could be alleviated.

With some trepidation I will venture into a controversial area to offer a hopefully positive suggestion. Criticism is frequently directed to the selection of test animals for extensive long-term studies and the subsequent extrapolation of the animal data back to man. To help answer this criticism we suggest that more frequent use be made of limited studies in human volunteers. Such investigations, which are already commonly carried out in pharmaceutical research and occasionally in pesticide research, elucidate the metabolism of a compound administered to man. Human metabolic pathways can then be compared with those of various animal species. A matching animal pathway will permit extensive investigation in that species and should correlate better with the events which occur in man. We would echo Dr. Coulston's general admonition, however: Please, no guidelines on this! At this time encourage it only and let us as individual companies pursue this approach as we can.

The fact that we are having this symposium is, we feel, a healthy sign and a positive action which we commend. Certainly the meetings that Drs. Axelrod, Korp, and Buckley have held with the Research Directors Committee of

NAC have been helpful and informative. Dr. Axelrod has patiently met with our committee on several occasions, has taken our views and concerns on the Alternative Chemicals Program into account, and has made a sincere effort to keep us informed. The mutual understanding eventually developed is an example of what can be done by cooperative endeavor and perseverance. Please keep up this activity. Don't quit talking to us even if we disagree now and then.

Summary

In summary, we in industry feel pesticides are and will be essential to food production and human health. We feel that the vast amount of work presently being done on new pesticides does establish safety and efficacy. We are attempting to monitor the pulse of the pesticide industry and feel that it is still healthy. Additional information will be forthcoming soon.

We are concerned about various regulations being promulgated but are encouraged by more recent drafts of some of these regulations. We reject totally any accusation that industrial scientists lack integrity or objectivity. As incentives we only ask that the regulatory system work as efficiently as possible and that in any review of registered products, each use be looked at individually. We urge that communications be strengthened to let us know if the safety or efficacy of one of our pesticides is being questioned. We would greatly appreciate help in developing reliable tests on genesis problems and urge that long-term feeding studies be at realistic dosages that do not exceed the metabolic capability of the test animals.

We are pleased that the cooperative field tour training program is getting under way. We suggest some modification of requirements for minor crops. We suggest that greater use of human volunteer studies would prove useful to compare metabolic pathways prior to chronic toxicity studies; and we urge that all communication lines among EPA, the academia world, and industry be maintained and nurtured.

RESEARCH AND SPECIAL CONSIDERATIONS: NONAGRICULTURAL USE PESTICIDES

Mr. Melvin Garbett*

The homeowner, like the farmer, is faced with the problems of pest. But unlike the farmer, the homeowner in most cases cannot identify his problems and in most cases doesn't get the expert advice to give him the help he needs. To most homeowners the whole concept of agriculture is a potted geranium. They don't have the knowledge of a specific crop and the specific problems that can occur. It's not a matter of "How do I control cabbage looper in my soybean field," but rather "My roses don't look so good, what can I do about it?" You ask, "What's wrong with them?" "I don't know — something's been chewing at the leaves." The sales clerk at K-Mart may or may not be of help. And by the way, this is who they often rely on for their help. Somebody has to provide solutions to their problems. State extension experts don't make house calls and we don't have enough local clinics to prescribe solutions to their specific problems. So what's being done to solve the homeowner's problems? Is industry participating? You bet it is!

We have taken on that responsibility. However, specific recommendations for specific problems are not the solution. The answer must be to provide products that do many jobs, offer broad-spectrum control with well defined, easy-to-follow label directions. We have to make it easy, not only for the user, but also for the person selling. Do you begin to see what we're up against? This is a very unique area in pesticide development.

As the homeowner's problems differ from the farmer's, our research efforts differ from those of agriculture. I'm not talking about spraying several acres of cotton or soybeans, but a few square feet of lawn. I'm not talking about aerial applications or row crop sprayers, but aerosol cans and 1-gallon Hudson sprayers. I'm not talking about producing 100 bushels per acre, but producing an environment of beauty. It is a different ballgame and a ballgame requiring a different set of rules — or another way of putting it — requiring special considerations.

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*Supervisor for the Garden and Home Research Department, Ortho Division, Chevron Chemical Company

The way I see it, the EPA rules and regulations are designed to do one thing: to prevent unreasonable adverse effects to man and the environment. As a member of industry and a private citizen, I can say that we support that 100 percent.

This support is reflected in our research efforts. Over the past several years we have identified and developed solutions to the problems facing the homeowner. As we put together products we are acting from a basis of knowledge, not solely on the basis of the almighty dollar. G&H pesticides are not arbitrarily put together. At Chevron, for example, we have a team of experts and experiment station facilities throughout the country continuously developing new and safer compounds, testing under controlled conditions, demonstrating under typical use situations, continuously improving products and making sure products continue to do the job they were designed to do. Can the effective dosage be reduced? Can we improve on the solvent system? And indeed, are they environmentally sound?

There's much work to be done on the older compounds and their effect on the environment. It's agreed they need to be updated, but within a reasonable time table. Let's not just simply discard them while determining their impact. There aren't really that many compounds available to the homeowner as it is. The supply has been greatly trimmed over the past few years.

Where are we heading? I hear stories about pest resistant varieties, possibly in the role of plant disease control. Cultural control? Biological control? Perhaps. But they have their limits as you well know. Bacillus thuringiensis gives control of certain lepidopterous larvae, but how do you tell a homeowner to apply between second and third larval instar? And some pests have few if any natural enemies, or those enemies do not act in time to prevent serious plant damage. Integrated control makes more sense — to include chemicals when needed but to use them sparingly and judiciously. The homeowner may never have heard the term "Integrated Control." He's not aware of it, but he is using it. He uses the pluck and squash method when he sees a caterpillar and sprays when he sees numerous caterpillars or extensive damage. He's not on a spray schedule like the farmer. The homeowner sprays intermittently, when needed, in small amounts — in most cases no more than 3 to 5 gallons of diluted spray per application and usually less. This again reenforces the fact that this is a different business from that of commercial agriculture.

Another responsibility taken on by industry is to help the homeowner make better use of the pesticides available to him. I can give you several examples:

- Easier to read and understand label directions
- Accurate applicators with automatic dilution ratios
- Pre-measured pesticides

Industry has the manpower and technology to provide better use of what we have. And we must continue to use it.

At the same time we must utilize our manpower and technology in developing new compounds and products for garden and home use. Do I have to bring up the tremendous pressures put on us by EPA to meet the requirements to register new compounds? An experimental permit to spray a rose bush! Data on Eastern tent caterpillar must be separated from that of the Forest tent caterpillar and each must be labeled separately! Approximately 50 percent of the label is taken up by cautions and warnings, leaving only a small portion to label use directions, pests, and hosts! Moreover, we're told that we can't recommend a particular product for a use not on the label, regardless of whether it's registered or not for that use! Don't get me wrong, cautions and warnings are important, but do we need to label our Sod Webworm Control with "This product is toxic to shrimp and crab"?

The enormous amounts of money and time required to meet these demands go without mention. You've heard it over and over again, but it does lead to a very important point. As there's a risk-benefit factor in the use of pesticides, there's also a risk-benefit factor in corporate decisions. Not too long ago, the Vice-President of Ortho asked me a simple question: "Should we be in the G&H pesticide industry 8 to 10 years from now or should we be looking into other ventures?" Well, the idea that something like this entered his mind scared the heck out of me. But risks such as product cancellation, alternate chemicals, relabeling problems, and inventories are nothing but headaches to corporate management. With the increased pressures from regulating agencies on our business, will management continue to appropriate funds for research and development, expansion, facilities, people, etc.? Will they continue to support research and development for minor crop uses with the risk being greater than the benefit? As I've already established, it is a risky business. How much will corporate management take?

While millions of dollars are being sunk in a relatively high-risk venture, the same dollars can often more safely be invested in the corporate stock or a less risky endeavor such as the panty hose business. Over the past few years we have seen several large corporations make the decision to "get out of" the G&H pesticide development business. Increased pressure on industry could cause additional companies to make that same decision. Inevitably having an effect on those companies surviving the pressures, it will lead to discouragement and a reduction in research for new, better, safer chemicals which will meet the rigid standards required in protecting the environment. What is needed more than ever are incentives. You've got to give them to us. Incentives that will encourage research not discourage it.

In summary, I would like to briefly reemphasize the four major points I have covered here today.

1. We must recognize the fact that the use and development of garden and home pesticides are greatly different from those of commercial agriculture.

2. Industry can supply the manpower, facilities, and technology to locate and solve the problems of minor crops, and we must continue to do so.

3. New and safer pesticides are needed for the future, and incentives need to be provided to ensure they will be there.

4. And most important, let's be sure to protect the old while developing the new.

MS. ROSMARIE VON RÜMKER: I wonder if you could be a little more specific on what incentives you would desire and how and by whom they should be provided.

MR. MELVIN GARBETT: By incentives I guess I really mean encouragement.

MS. VON RÜMKER: Encouragement from whom — from the consumers or from the governments or . . .

MR. GARBETT: No, from the regulating agencies of EPA.

MS. VON RÜMKER: Well, by words or by what? How should . . .

MR. GARBETT: Okay, here's an example. For instance, we want to provide the homeowner with easy-to-read and easy-to-follow label directions. Presently when we label a product we have to label a specific insect for a specific plant, such as aphid on rose. Now to do that with every insect on every plant that we would like labeled, we would have to include an encyclopedia with the product.

So what I have proposed is that we can list in one column the insects where we have efficacy data, and in then another column we can list the plants that are attacked and where we have phytotoxicity data, rather than a particular insect for a particular plant. As far as I'm concerned, and I think I can speak for the CSMA, the ultimate label for garden and home use, is that "This product controls insects on your plants." We'll never achieve that, but it's a goal. This is the sort of thing I'm talking about when I say "incentives" — an easing in regulations that will encourage further development of garden and home pesticides.

THE FUTURE OF PESTICIDE RESEARCH: A CHALLENGE

Leonard R. Axelrod, Ph. D. *

International research considerations began with discussions by Dr. Lu and Dr. Turtle, and a broad spectrum of academia and government was brought into play; Dr. Alder brought in the myriad of research needs of industry, not only to comply with government regulations but also to contribute to the development of new pesticides.

I should like to discuss the world of pesticide research, which to me is an exceptional challenge, and I think I have the naiveté of a newcomer to be able to think in a rather broad spectrum of possibilities. I hope that when I'm finished, you will be able to walk out and say to yourself, "Why that was perfectly obvious." That would mean that we are thinking innovatively of the possibilities for the future.

The introduction of biologically derived materials for the control of pests, such as viruses, bacteria, juvenile hormones, growth hormones, pheromones, parasites, and predators, represents the "new generation pesticides." For these materials, "tomorrow is already here." Thousands of man-years have been devoted to research on the development, synthesis, safety, and efficacy of most of these instruments of control. Inevitably, many, if not most, will be registered and incorporated into the arsenal of those who labor for the protection and production of our food and feed, the agricultural community.

Today, however, I would like to go somewhat beyond the many so-called "new generation pesticides." Today, I would like to voice some lateral thoughts in an abbreviated synopsis primarily to provoke thoughts and discussion, because "tomorrow is already here" in the need for innovative and lateral thoughts in the field of pesticides.

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The fervent hope is that all concepts are "perfectly obvious" and that the future of pesticides can be anticipated. Pesticides, however, are only part of the story. An overall look at our civilization must be taken first to discern just where pesticides fit into the picture. The future of our society will be shaped by many things.

It will be shaped by many different technologies which break down simultaneously; it will be shaped by many crises which will occur and which may be of magnitude greater than that which has been coped with in the past.

It will be shaped by the fact that pollution and technology tend to grow exponentially and in parallel, so that critical problems and subsequent damage may occur before cognizance of such damage is anticipated and is prevented.

It will be shaped by the interpretation of human values in our culture, the unifying concern for long-term human survival.

It will be shaped by physical operational parameters for our planet, that is, the ecological or housekeeping rules that govern human occupancy.

It will be shaped by the contextural interplay of fear, affluence, standards of living, and population among our societies and nations.

It will be shaped by our evaluation of priorities in the utilization of energy, human and physical.

It will be shaped by the availability and distribution of agricultural products.

It is the last point that is the primary focus of this discussion. Although all the others impact directly upon how the goals are achieved and the priorities assessed, it is my considered opinion that the field of pesticides as applied internationally must depend on a multifaceted approach, innovatively, to the subject of pest control, and that this approach must include new broad-spectrum fundamental scientific research in order to cope with the insects and plants that have genetically "tuned for survival" for more than a billion years; and I might say that the rodents, which have not been here as long, have also contributed greatly to the destruction of our food and feed.

Unfortunately, it is now the ebbtide of technology in areas of agriculture. It was the years of 1940 through 1960 and the years at the turn of the century which gave great advantage to the emerging agricultural community; from the harvester machines and other mechanically complex systems to the serendipic discovery of chemicals like DDT, the "panacea" of the agricultural world at one time, as penicillin was to the pharmaceutical world.

Corn production has risen from 26 bushels per acre to 91, (somewhat less — 76 — this year). Nevertheless, you can only produce so many bushels per acre with our present technology. The bugs, the weeds, and the rodents control 20 to 25 percent of our produce.

It is time to look ahead on a broad-spectrum analysis which will require human resources, funds, and above all, the capacity to think.

The following are some avenues of pesticide research for pest management and are presented for your consideration and thought.

The insect has been here at least one billion years. The plants (algae), interestingly enough, have been shown recently to have been here three and one-half billion years. Their capabilities at a molecular level to survive and adapt are legion. DDT was introduced about 1944 and this morning my colleague, Dr. Fred Whittemore , tells me that by 1948 the housefly was resistant. As DDT was used, it became obvious that more and more was necessary to control the pests and that finally the resistance was at a point where it was neither economically nor environmentally feasible to continue.

I submit the following:

1. The introduction of extremely toxic pesticides — pesticides that make TEPP look toxicologically like jello. In the same package, however, the internal

controls will be present simultaneously, perhaps by utilization of methods such as microencapsulation and time-release systems for nullifying (detoxifying and inactivating chemically) the hazardous effect of the active ingredient.

Footnote for the manufacturers: Please don't throw out the compounds you don't have on the shelves.

2. Much has been said about the contamination of our soils, air, and water with pesticides that have been applied unjudiciously in the hopes of a better agricultural return. It is time to think about the development of chemicals and techniques to inactivate the hazardous effects of pesticides already on the landscape and in the air and water — a definite public health mission.

3. It is time to consider the rhythms and cycles of the insects and plants the circadian rhythms, the time clocks — diurnal, nocturnal, and crepuscular.

It is time to consider the reproductive cycles of insects, which are controlled by time, weather, temperatures, and chemicals.

I suggest alteration in specific food selectivity by changing the plant (host) metabolism, that is, the relationship between the almost parasitic dependence of an insect species upon its selected food composition, including smell, taste, color, and pH. If the insect wakes up at the wrong time, before the food is ready or after the food composition has changed (e.g., sugar to starch) which represents to the insect that special taste, smell, color, or pH, you have disrupted the parasitic-host cycle relationship and that is a method of control. It is not an accident that tomatoes are not attacked by the Japanese beetle but other plants next to them are. It's also not an accident that plant leaves in the garden are burned just by proximity to certain other plants in the vicinity.

5. On the other hand, the alteration of the insect's color and smell to attract predators can also be utilized.

6. I suggest the development of plant strains of nutritive value that thrive upon presently considered air, soil, and water pollutants. We had an excellent exposition by Dr. Kearny who discussed changing plant species for resistance to insects. The metabolism of plants can also be altered to accept, as part of their nutrition, such pollutants. We know about sulphur bacteria. In my own laboratory, we had mold growing in pure sulphuric acid. It did not change the nutrient value of that mold as far as its protein went. We examined it just out of curiosity one day about 18 years ago.

Therefore, seek to clean the environment by the use of plants and animal species that act as sumps for the pollutants and by the use of microbial and submicrobial evolved species to harvest these pollutants out of the fresh waters and even out of the ocean. After all, there is no greater chemist or adsorbant than life. There is no greater adapter than the genetic code. Use these changes to destroy the pollutants by harvesting animal and plant life adjusted to thrive on these pollutants.

7. Develop equaticnal precepts that relate optimal energy expenditures to crop growth and uses and to food chain goals. I think the economists might have a place here, as well as the physical and biochemical scientists.

8. Perhaps what may also be necessary is the alteration of national palates for nutrition rather than mere taste (e.g., "good" instead of "prime" beef). This could require a reassessment of priority needs in our affluent societies.

It is time for innovative thinking and discovery. It is time for young and audacious minds to enter the field of pesticide research.

There are at present fine scientists and innovators in pesticide research, but they are taken up by the innovations of yesterday and the pragmatism of today. We need new people, products of the heritage of agricultural communities and pesticide research, who will enter into this fracas, into the challenge of pesticide research.

We cannot seek a panacea. There is no magic compound. Penicillin was not magic and neither was DDT. They existed in a moment in time and all but disappeared. We will not be able to use exclusively juvenile hormones or pheromones or viruses on 78,000,000 acres of corn or 17,000,000 acres of cotton. The problems need broad-spectrum thinking and integration of thoughts, one with the other, in the areas we've delineated and in many more, which I'm sure that you've thought about. But the time to begin is now; it's really yesterday for starting the process.

The discoveries of the 15th and 16th centuries were placed literally into orbit by our space program. The equations developed for space were not by computers, they were by thinking men in those earlier centuries. Even Dr. Einstein's hypothesis of mass and energy published in 1905 was not proven until 1919. He was lucky; that's a relatively few years in science for going from the "drawing board" to the "proof" and the pragmatic application of atomic energy today.

We are as someone in outer space — looking back; you see many problems but they appear miniature, because none of us can see the particulars of the whole or what the future will bring. The ideas you put forth today which will be considered for life on this planet will also alter our ideas of how to deal with these pesticide problems.

PESTICIDES RESEARCH IN THE ENVIRONMENTAL PROTECTION AGENCY:

INTRODUCTION

John L. Buckley, Ph. D. *

I'd like to welcome you to the last of our sessions here. What I want to say at the outset is that we in EPA in the research area are kind of a diverse group. We came from various places when EPA was formed, and we've had various perspectives and various ways of doing business based on the different sections of the government that we had been associated with. I don't want to make a long history of this, but I do want to call your attention to the fact that one of the units brought into the EPA was a single unit out of the Bureau of Commercial Fisheries in the Department of the Interior. All the rest of that Bureau went to the Department of Commerce, but Tom Duke in Gulf Breeze, Florida came to EPA. The Federal Water Quality Administration (FWQA) in the Department of the Interior also came to EPA.

FWQA had a number of laboratories working on water pollution, and among the substances that they dealt with were a number of pesticides. I would like the record to clearly show that we don't look on pesticides in any general sense in EPA as being pollutants, but when in fact they're in the wrong place or when in fact the manufacturer's waste enters the environment, the pesticides like other biologically active materials are pollutants.

The laboratories in EPA that came from FWQA that were associated in some fashion or other with pesticides were the National Water Quality Laboratory in Duluth, Minnesota, the Marine Water Quality Laboratory in Narraganset, Rhode Island, and our Southeast laboratory in Athens, Georgia. The Athens laboratory

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*Acting Deputy Administrator for Program Integration, U. S. Environmental Protection Agency has continued, as has the Duluth laboratory, to deal in some fashion or other with research on pesticides. The Athens laboratory has been working in terms of measurement of methodology and in terms of fate of substances in the environment. The laboratory in Duluth has been concerned with the effects of pesticides — the acute and chronic toxicities to fish and other aquatic organisms for many years. The laboratory in Cincinnati, which also came from that group, has been involved in surveys of the presence of pesticides in water.

Another large unit concerned with pesticides research that came to EPA was the group from the Food and Drug Administration. That included the Perrine Laboratory, the Chamblee Laboratory, and the Wenatchee Field Station.

In addition to these rather discreet units, there were some others which impinged in one way or another and are sometimes forgotten. The National Center for Toxicological Research was invented, if you will, by the Secretary's Commission on Pesticides, which was chaired by Emil Mrak. When EPA was formed the Executive Branch concluded that it would be well for that concept to go forward, but for the funding and support of its programs to be the joint responsibility of EPA and the Food and Drug Administration. So in the first year FDA was given the responsibility and EPA was given the money that was set aside for this. This arrangement led to real close cooperation in the first year. FDA had the management and the laboratories but they didn't have the funds. So we did have a considerable influence from EPA on the structure, the initial thoughts, the management systems, and the other things which went into this.

Another unit which was transferred was the Secretary's Advisory Committee on Pesticides, and Emil Mrak and those people who were on the Commission at that point in time were moved to EPA and became responsible to the EPA Administrator as an advisory group. This group was renamed the Hazardous Materials Advisory Committee. Other groups transferred to EPA included the staff for that committee, as well as the staff for the Federal Committee on Pest Control.

The point behind all this information is really that because of these diverse origins, there were, in fact, various points of view. I wouldn't want you to think that we all sit here today with an absolutely uniform view of things, but we see more uniformly now than we did in the past the goals and objectives and the ways in which to achieve them.

In addition, I would also like to point out in this introduction that in regard to research directions, it is our view that the development and/or the evaluation of new and better methods of evaluating safety in all its aspects is perhaps our major responsibility.

We think and the law clearly specifies that the major responsibility for the provision of data rests with industry, and in no way do we wish to take on that responsibility. On the other hand, we do feel a deep responsibility to improve the ways in which data can be generated and the means by which data can be synthesized and evaluated. We've been working on this in a number of ways.

The second responsibility we have, it seems to me, is to produce data needed for understanding of a problem when such data are not otherwise available.

There are a number of situations in which this is clearly the case. For example, in analytical chemistry there are times we wish to look for a number of substances in foods or in other substrates. The substances are clearly not the responsibility of any one industry, and we find it advantageous to develop methods for these. There are compounds on which information is desired, the patent period has run out, and there is no proprietary interest. It would be nice if there was somebody we could turn to for that additional information, but there are cases in which this is not so, and you know them better than I.

We have a small program that is concerned with what we call alternative methods of pest control, which I mentioned the other day. Of approximately $8 million in research, including the monies that we're responsible for under the

Alternative Chemicals Programs, approximately $1.8 million goes into this matter of development of alternative methods of pest control. A large part of that has been for the support for the so-called Hufaker Project — a large number of universities and investigators working on non-chemical control methods and integrated methods in a number of crops.

We have been in one way or another in the pesticide research business for quite a number of years. The funds associated with the Alternative Chemicals Program have somewhat narrower and more specific objectives than the other funds that we have used and are using. They are not a dominant part of our program in terms of total monies available. They are, in fact, an important part of our program, and we hope to work very closely with you in the expenditure of these monies in the sense of not duplicating what's already done. We may have occasion to validate data. We may have occasion to do some things that you believe are already done. However, we have no desire to generate data that you already have.

OVERVIEW OF ECOLOGICAL EFFECTS

Norman Glass, Ph. D. *

Let me begin by saying that this program is relatively new. In fact it has only recently begun in the last 2 or 3 months. We received our initial funding in May or June of this year, and I should point out for those of you who haven't already read it in the program, that we'll be dealing with the ecological effects aspects of the Substitute Chemicals Program.

The ecological aspects of this program have been developed on the basis of the historical and resident expertise at a number of the research laboratories from the National Environmental Research Center in Corvallis. In fact, four of the laboratories represent this center on the Substitute Chemicals Program, and I would like now to introduce the panelists and identify which laboratories they're with and what their general areas of responsibility are.

The four laboratories are represented first by Dr. Jim Gillett, whose detailed biographical material is in your program. Dr. Gillett is from the National Ecological Research Laboratory. He is basically a biochemist who has been involved in pesticide research for many years. He's also responsible for putting together the terrestrial aspects of the program.

Next to him is Dr. Thomas Duke, the Director of the Gulf Breeze Environmental Research Laboratory in Gulf Breeze, Florida, whose responsibility is in the estuarine and the marine effects area.

Next to him is Mr. John Eaton from the National Water Quality Laboratory whose responsibility is in fresh water toxicity or toxicological data development in the fresh water environment.

Mr. Jim Hill, from the Southeast Environmental Research Laboratory in Athens, Georgia, is responsible for discussing the fresh water transport of pesticides.

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*Director, National Ecological Research Laboratory, U. S. Environmental Protection Agency

My function in this is largely to oversee the ecological effects area and to try to minimize the number of gaping holes in our knowledge that crop up in that area.

Having briefly introduced each of the panelists, let me give you a quick rundown on the nature of this program as we have seen it. First, as I mentioned, the program has just begun, but it has two distinct but very related parts. The first consists of a conceptual framework or a planning document which describes the way in which all of the various pieces of the program fit together. This basically could be called a conceptual model, although I would really like to minimize the model aspect in favor of emphasizing the thought or the framework within which we can all perform a research program.

The second major portion of the program is a methods development phase which involves the use and development of microcosms as testing methods or as testing procedures for evaluating or assessing either new or existing pesticides.

In our overall compartmental type model, there are several general categories we will be working in. These include the atmosphere, the land, fresh water, estuarine waters and marine waters, and the sediments and other terrestrial components of each of those compartments. Within each of these categories there is a further breakdown into what we consider most important, namely the biota which exist in each of those compartments and the various feedbacks and transports and directional flows of material through the compartments and among the biota.

Our conceptual framework is in the nature of a compartmental model which we can break down into program bites, so to speak, which each laboratory is then free to deal with as an integrated problem. We then integrate the entire problem into a holistic view of the way in which pesticides move through the environment and possibly what some of their effects are.

Now, as most of you probably know, the microcosm methodology which we are developing is a relatively new type of research and I'd like to emphasize at this point that even if it were not new and even if it were completely developed, tested, and validated, it would still not represent the ultimate in screening procedures or assessment methods which would be used in the registration process to evaluate a pesticide.

This is only one piece of data which has to go into pesticide evaluation. Microcosms also offer the advantage of being relatively inexpensive, rapid, possibly turn-key testing methods as the years unfold and the methods become better developed, but I would like to emphasize that they are at this time extremely rudimentary and clearly in a developmental phase.

In closing, the substitute chemicals which we are investigating under this program obviously exhibit or may exhibit many properties that are quite similar to conventional pesticides or, let's say, more thoroughly understood pesticides. They have properties such as bioconcentration, biomagnification, biological transport through food chains, and biodegradation. It is because of the presence of and the need to study the many environmental routes, rates, sinks, and effects of a variety of substances proposed as substitutes for banned or deregistered pesticides that we have developed this program.

TERRESTRIAL EFFECTS

James Gillett, Ph.D. *

We have two basic aspects along which we are proceeding as Dr. Glass has stated. First, we have been concentrating on the development of the conceptual model of the interrelationships of terrestrial systems to aquatic systems, and second, we have been developing methods or approaches using terrestrial microcosms. We have not proceeded very far on the second, because we are a very new program. We are just moving into new laboratories that will be functioning by the middle of September or maybe early October.

Then we will move into trying to develop chambers which we can characterize — which we can develop as an array of biological and physical conditions or components that will represent conceptually, in a way, an organism that is a little more complex in some regards than a given species, but not as complex as an actual ecosystem. I refer to these as microcosms and not as model ecosystems, because they are totally dependent on our input, our characterization, and our design. We believe that in a few months, to hopefully not more than a few short years, we will have available arrays (representing environmental conditions, certain types of croplands, or certain types of environmental situations) which will allow the rather rapid evaluation of the disposition and consequent effects of the release — intentional or accidental, adventitious or otherwise – of a pesticidal agent or similar compound into the environment.

In order to do this and make it a valid approach, it is my contention that we must go back to that conceptual model and bring it along with our methodology. That is, we must develop explicit chemical models, biological models, and interrelated microcosm models and bring to bear systems analysis, computer simulation, and explicit physical, chemical, and biological characterization of these chambers to give rigorous scientific approaches to analyzing these kinds of problems.

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*Ecologist, National Ecological Research Laboratory, U.S. Environmental Protection Agency

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If we had not been successful in other areas at other points in time, I would say that this would be a hopeless task. However, I am very much persuaded that we can accomplish our goals. We have had some very good success in modeling other environmental releases and modeling pharmacokinetics within animals. In part our success will depend on maintaining cooperation and the kind of thinking that Jim Hill characterized in one of our meetings on the conceptual model. Each laboratory can bring forth something new, not just in terms of a disciplinary effort. As we take from the process end and take from the systems end, then meld them together, we can develop the holistic approach that Dr. Glass has emphasized. It will not be easy and I cannot guarantee success by a certain date, but I think we can make real progress. We have seen it internally, and I hope we will be able to communicate some of those results to you in a hard document within the next few weeks.

MARINE LIFE

Thomas W. Duke, Ph.D. *

Pesticide residues occur in biotic and abiotic components of coastal and oceanic environments, and some of these residues have been implicated in degradation of portions of these environments. Many pesticides can be detected in tissues of organisms at the parts per trillion level, but the effects of such levels on the organisms and systems in which they occur are not clear in many instances. Knowledge of these effects is especially important when the residues occur in the coastal environment which is a dynamic, highly productive system where freshwater from rivers meets with saltwater from the sea. The coastal zone interfaces with man's activities on land and, therefore, is especially susceptible to exposure to acute doses of degradable pesticides as well as chronic doses of persistent ones.

Many species are important as human food and spend part or all of their life cycles in estuaries. It is important, therefore, to study the effects of pesticides on these animals in estuaries where they are most likely to contact toxicants for the first time. Our laboratory is well situated for this study, being located on a large estuary that has more than 100 square miles of varied habitats and empties into the Gulf of Mexico. The Gulf of Mexico is the site of shrimp and menhaden fisheries, the nation's chief fisheries in terms of income and volume. Approximately 90 percent of all commercial fishery organisms in the Gulf of Mexico spend at least a portion of their life cycles in estuaries.

The purpose of this talk is to give you a brief overview of our research activities with emphasis on our work with communities and ecosystems as they pertain to the Alternative Chemicals Program.

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* Director, Gulf Breeze Environmental Research Laboratory, U.S. Environmental Protection Agency

A toxic chemical can affect biological resources in two ways: (1) a direct effect of the chemical on organisms and (2) residues accumulated in organisms could render these organisms unsuitable for human consumption, thereby interrupting the supply of the resource to the consumer. At the Gulf Breeze Laboratory, we study the effect of pesticides and other toxic organics on marine organisms in the marine environment in which they live. We maintain a close relationship with the Estuarine Monitoring Program in the Office of Pesticide Programs, so that we may determine the kinds and levels of chemicals to use in our toxicity studies.

We determine the effect of these chemicals on various marine organisms such as plants, shrimp, crabs, oysters, and fish under controlled conditions in the laboratory, under semicontrolled conditions in experimental tanks, and in field tests in a natural environment. Laboratory bioassays, both acute and chronic in nature, use oysters, blue crabs, shrimp, and various fish tested in flowing water to predict whether a specific pesticide would be likely to damage an estuary when it is used in or near it. Of the test organisms, shrimp are usually the most sensitive to insecticides. Knowledge of how their physiology is altered by pesticides and where the toxicants accumulate in their bodies contributes to understanding the mechanisms of actions of these compounds. Also under investigation are their tolerance to toxicants and how these chemicals alter fundamental physiological processes and cause physical damage to specific tissues and organs.

Certain patterns of behavior are essential to the continued existence of populations of fishes and other estuarine animals. Alteration of basic behavioral patterns by sublethal concentrations of pesticides in the environment may subject the animals to increased predation or to intolerable physiological stress at critical stages in their life history. Certain pesticides have been shown to alter salinity preference of specific fish.

Testing of the effect of pesticides on embryological development and life history of the sheepshead minnow, a common fish in marsh drainage ditches, is now complete. Methods of rearing the embryos are being standardized in preparation for future testing.

Exposure to acutely toxic concentrations of pesticides usually causes rapid paralysis or death, but effects of long-term exposure to sublethal concentrations are often much more subtle. The damage may be hidden within specific organisms at the tissue or cellular level. Therefore, a staff pathologist is investigating pesticide-induced pathogenesis in estuarine animals.

Few data are available concerning the effects of pesticides at the ecosystem or community level of organization. This is not surprising considering the complexities of ecosystems and our lack of knowledge of the structure and function of coastal zones. Effects of pesticides could be masked by variations in population densities and it would require several years to evaluate such variations. However, it is possible to design laboratory and field experiments to yield information on this complex system.

Mr. David Hansen of our laboratory has worked with an experimental community that received 10 micrograms/liter of a polychlorinated biphenyl and the community did not recover to a "normal state" in terms of numbers of phyla and species after 4 months. Communities of planktonic larvae were allowed to develop in control aquaria and in aquaria that received the PCB. Communities that received 10 micrograms per liter of the chemical were dominated by tunicates, whereas controls were dominated by arthropods. The Shannon-Weaver species diversity index was not altered by PCB, but numbers of phyla, species, and individuals decreased.

In another experiment, Dr. Gerald Walsh and others of our laboratory introduced a herbicide into a small pond near our laboratory on Santa Rosa Island. Applied as a wettable powder in a concentration of one part per million, the herbicide eliminated the rooted plants in the pond. As the benthic plants died, blooms of phytoplankton and zooplankton occurred and a normal oxygen regime was maintained. As benthic plants returned, the number of plankters dropped. The pond returned to a "normal state" in reference to the primary producers approximately 3 months after treatment. Such observations, obviously, could not have been made in bioassays with a single species under controlled laboratory conditions.

We are cooperating with Dr. Norman Glass of the National Ecological Research Laboratory in Corvallis to determine the impact of pesticides on our "total" ecosystem. We are conducting experiments on the estuarine and marine portions of the system. To date, we have supplied information for a conceptual model of such an effect. Also, we have begun studies to establish a marine microcosm which we can use to determine the impact of a pesticide on the marine system. As you probably know, at present there are no standard methods for determining the impact of a pollutant on a marine ecosystem. We are experimenting with different types of systems and with criteria for determining impacts on these systems.

FRESH WATER EFFECTS

John G. Eaton*

I'd like to start off with the disclaimer that most of our work has had an orientation distinctly different from that which has been discussed or presented here at the meeting so far. To reiterate some of the things that John Buckley said, most of our work has been done in response to requests or a need for water quality criteria to derive water quality standards. Water quality standards allow the introduction into water of various toxicants, pollutants, or other compounds up to specified levels or concentrations. The objectives that we have followed in obtaining these criteria values might be entirely different from those we might set if the primary orientation were, say, pesticide registration, so please keep this in mind.

First, although I realize that this might be repetitious to you who have heard me speak before, I'd like to give you some idea of the scope of our laboratory's activities. These activities are by no means limited to the study of pesticides. As a matter of fact, pesticides research is a small part of our program.

Our base laboratory, which is also our largest laboratory, is the National Water Quality Laboratory in Duluth, Minnesota. It's located on a 13-acre tract of land on the shore of Lake Superior and was completed in July of 1967. Dr. Donald Mount is Director of the Laboratory. It consists of a main building having approximately 54,000 square feet of floor space, and about half of this is chemistry and biology laboratory space. Approximately 75 people work there.

In addition to this laboratory, we have three field stations throughout the country. The Newtown Fish Toxicology Station has been in operation since 1961 and is located near Cincinnati, Ohio on the grounds of a State Fish Hatchery.

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*Coordinator, Pesticides Research, National Water Quality Laboratory

About eight people are employed here. They recently conducted a 3-year field study in which copper sulphate was metered into a 1/2-mile stretch of natural stream in order to compare its effects in nature with those observed in several prior and concurrent laboratory chronic exposures.

Another field station, the Western Fish Toxicology Station, is located in Corvallis, Oregon. The building there has 12,000 square feet of floor space and facilities for exposing large adult Pacific salmon to toxicants. The major research emphases at this laboratory are on the effects of supersaturation and heavy metals on aquatic organisms and on test method development.

The third field station is located at the site of the Monticello, Minnesota nuclear power generating facility about 20 miles north of Minneapolis on the Mississippi River. The station consists of eight earthen channels, 16,000 feet long by 20 feet wide, and a small fish-holding and staff and facility support building. Initially the channels will be used for the study of thermal effects on fish and aquatic invertebrates, but subsequently they will probably be used for toxicant exposures. The site was chosen so that it could use the waste heat from the nuclear power generating facilities. It has been calculated that it would cost up to $10,000 per day to otherwise heat the water in the channels.

Nearly all our pesticide research has been done at the Newtown laboratory, at the Duluth laboratory, through grants and contracts, or through interagency agreements with the Department of the Interior.

One of the most important accomplishments of the National Water Quality Laboratory has been the development of life-cycle chronic test procedures and acute testing procedures for several species of fish and aquatic invertebrates. These permit evaluation in the laboratory of the effects of toxicants on all aquatic stages of these organisms, including reproduction. These procedures are now being used in many other aquatic research laboratories besides our own. Several research contracts have been completed and others are underway, involving use of these methods for the study of the chronic toxicity of pesticides and other compounds and resulting in improvements and modifications. We are continually working to improve these methods and to devise new ones for additional aquatic species.

Through the use of both short- and long-term tests we have determined or are in the process of determining the acute and chronic toxicities of compounds which include 2,4-D, copper sulfate, organic and inorganic mercury, atrazine, guthion, malathion, diazinon, chlordane, toxaphene, methoxychlor, heptachlor, lindane, parathion, treflan, captan, several PCB's, DDT, sevin, baygon, fenthion, propachlor, methomyl, mirex, triton X-100, acetone triethylene-glycol, dimethylformamide, and phthalates. The values derived are used in attempts to estimate what we call water quality criteria or the quantitative estimates of detrimental effects to be expected from different levels of environmental contamination. The criteria are in turn used to derive water quality standards or values defined by governmental authority as concentrations not to be exceeded. Many of the toxicity values from our studies have been cited in the document entitled "Water Quality Criteria" prepared by the NAS under contract to EPA. Among the more urgent research needs identified by the NAS was the need for additional data on chronic effects of toxicants and on additional organisms.

Currently we are reviewing a water quality criteria document being prepared by the EPA itself, which will include data made available since the NAS publication was completed 3 years ago. Such criteria evaluations are extremely difficult and are largely only educated guesses because they must consider, besides observed effects, sensitivities of untested organisms, interactions with other environmental toxicants or factors, and potential effects of associated residues on other aquatic life, terrestrial wildlife, or man. Communication and cooperation is therefore necessary among investigators and laboratories representing several different areas of specialization.

The National Water Quality Laboratory's data and expertise were also utilized recently in testimony on behalf of proposed EPA effluent standards. Compounds on the initial list of nine compounds for which we provided toxicity information or prepared affidavits were endrin, toxaphene, PCB's, cadmium, and mercury. As the safety or harmfulness of effluents must ultimately be determined on the basic effects of concentrations of effluents in receiving waters, essentially the same data base is used to derive effluent standards as is used for water quality criteria.

We have also been involved to a limited extent in aquatic environment residue-assessment studies, such as monitoring pesticide and PCB residues in fish from Lakes Michigan and Superior. We are occasionally asked by outside groups to assist in identifying or quantifying residues in fish tissues sent to us from around the country. These studies often require that we modify existing analytical techniques or devise new ones. In monitoring the concentrations of pollutants in our laboratory exposure systems we frequently have to measure very low levels because of the extreme sensitivities of the exposed organisms. For example, we are talking about levels such as 0.1 ppb or diazinon in water or 0.06 ppb of toxaphene. As shown by water quality criteria for aquatic life in comparison to the drinking water standards for several pollutants, drinking water levels for pesticides frequently will not protect aquatic organisms. Many of the residues or breakdown products we attempt to identify have never been investigated before as far as we can ascertain, and no methods are available for them. Thus we must have a well equipped and highly competent analytical chemistry section.

Chronic effects we have observed have been extremely diverse and have included lack of reproduction, reproduction but inability of the eggs to hatch, crippling of embryos, crippling of fry, crippling of adults, reduced growth, reduced survival, tendency to convulse, lethargy, hyperactivity, increased aggression, avoidance, and many combinations of these. In the case of some toxicants, fish have proven more sensitive than invertebrates and vise-versa. These considerations make it essentially impossible to estimate safe levels of toxicants without conducting some long-term exposures with more than one species. The big question, of course, is how many exposures. In the absence of any chronic toxicity data, acute values have been used in the past by multiplying them by arbitrary application factors to provide estimates of chronic toxicity, 1/10 or 1/20 being the factors often used in the case of degradable or cumulative compounds and 1/20 or 1/100 in the case of persistent ones. Experimentally derived application factors, that is factors obtained by dividing experimentally determined chronic toxicity values by acute toxicity values, have been found to vary greatly. Factors ranging all the way from about 1/3 to 1/3000 have been observed. We have often found that the greatest difference between the acute and chronic toxicity values does not occur in the case of the more persistent compounds. Application factors of 1/50 for malathion and 1/1000 for diazinon induce residue BMF's of only about 20 and 25 times, respectively. For lindane and endrin, on the other hand, which are more persistent, we have observed AF's of 1/3 and 1/4, but residue BMF's of 500 and 15,000 times, respectively. Thus a tendency to bioaccumulate is not a good indicator of chronic toxicity potential to be used when trying to guess safe levels from acute values.

Naturally, the use of experimentally determined chronic test values is preferred in developing pesticide water quality criteria. However, it is obviously impossible to determine sensitivities of all aquatic organisms. One alternative is to find a means of extrapolating from chronic effects on a few organisms to chronic effects on others for a given toxicant. Test results to date with fish have indicated that the ratios of acute to chronic test values for several fish species exposed to a given toxicant are in many cases similar. With some compounds, however, the ratios have not been very close, indicating that the reliability of extrapolating to chronic safe values from acute test results is comparably reduced. Such estimates are still much better than those derived through use of completely arbitrary application factors. We are presently making a major effort to evaluate the predictive capacity of this AF concept by critically reviewing 30 or 40 sets of chronic and acute toxicity data. We hope to publish the results of this review in the fall or winter.

We have frequently found that invertebrate fish food organisms are more sensitive chronically to pesticides than are fish. Thus the crustaceans and aquatic insects appear almost uniformly very sensitive to organophosphates, but several exceptions exist that dictate the necessity of testing other types of organisms also.

We have also investigated biochemical and behavioral methods of estimating chronic toxicity from short-term exposures. Many chemical indicators have proven useful in specific instances, but are of limited use because the indicators, often an enzyme or blood constituent, usually respond to only a single toxicant. Others such as ACHE respond so generally as to be of limited value for extrapolations because of wide species variability.

A behavioral response we are working on which appears promising is the use of the cough response of fish. This is a rhythmic back-flushing of the gills of fish which normally occurs every minute or so. When exposed to toxicants above a certain threshold level, the rate of coughing increases, and it has been observed that this threshold level often corresponds remarkably closely with the concentrations determined to be "just safe" in long-term chronic exposures. Thus for brook trout, the cough frequency response concentration and the "just safe" chronic toxicity concentration are 9 and 6 ppb respectively for lindane, 8 and 7 ppb for malathion, and somewhat less than 10 and 25 for diazinon. The recording of the cough response is accomplished remotely using a physiograph, and while the fish can be left in the detection chambers for weeks or even months, the determination of threshold levels usually takes only a few days. The predictive possibilities of this system could be great and might extend to complexes or mixtures of toxicants as well.

Another interesting study we have just completed looked at the relative contributions of DDT-contaminated food and water to chronic toxicity and tissue residues. Fathead minnows were exposed to DDT in water at concentrations near the chronic toxicity threshold. Half the fish were fed ground clams that had been exposed to the same DDT concentrations as the fish, and half the fish were fed uncontaminated clams. The DDT exposed clams had an equilibrium level of 45 ug/g of DDT residues in their tissues or about 25,000 times the exposure concentration. In addition, the DDT in the clams was radio-isotope labeled so that in the minnows the fraction of the DDT coming from the food could be differentiated from the DDT picked up from the water. Clams were used as a food source because they provided a large amount of food tissue into which we could metabolically incorporate DDT residues.

Some of the conclusions from this study were that DDT in the food as well as the water did increase residues in the minnows and increased the toxicity proportionally. The significance of the contribution due to food was greater at lower water concentrations, however. Similar responses were also observed in second generation fish with no apparent increases in toxicity. Some interesting and as yet unexplainable observations were made on some of the adult fish that were placed in clean water after termination of the experiment. There was a fairly rapid elimination of the labeled or food source DDT, but the DDT residues from the water source changed very little within 56 days. This was not attributable to differences in the analogues between the two sources because all the food source analogues we excreted at an equal rate. Nor did it seem to be due to differences in storage sites of the two different-source fractions, as several tissues contained the same proportions of labeled and unlabeled DDT. In general, this study provides some interesting implications in regard to the conducting of chronic exposures with persistent pesticides. To get a better handle on these we plan to start a similar study with another chlorinated hydrocarbon with different residue properties in the near future.

Along similar lines, we have recently observed that the pesticide mirex is much more toxic to aquatic invertebrates when they ingest the pesticide than when they are exposed to it in water alone.

Other areas in which we are conducting pesticide research are on the techniques for studying interactions of mixtures of pesticides, the toxicity of intermittent or fluctuating concentrations as compared to continuous concentrations of pesticides, the toxicity of breakdown products and metabolites, and the use of simulated ecosystems to quantitatively determine effects not just fate and transport of pesticides.

In conclusion, I would like to say that we are in full agreement with the projects and objectives of the Alternative Chemicals Program. Therefore, we are anxious to cooperate in the program and to be of assistance in any way we can.

PRELIMINARY SYSTEMS ANALYSIS AS A TOOL FOR DESIGN OF RESEARCH PROGRAMS

Mr. James Hill, IV*

To put things in proper perspective, I'm going to talk about a research tool, which is at the bottom of Dr. Axelrod's mountains — but that's not of concern to me because without the foundation there are not going to be any mountains. There has been a theme running through the symposium which is presented in some of these short quotes: "The subtle effect of pesticides," "hidden devils," "secondary effects," "adverse effects on processes," "the network of roads through plants and animals to man," and finally "diethylstibesterol affecting emphysema in California." All of these quotes refer to system components acting in concert to produce "subtle" or "hidden" behavior. All system behavior is related to three system processes that describe everything that happens in any system — transport, transformation, and storage. Anything that happens with respect to any material can be described in terms of these three basic processes.

I don't know much about alternative chemicals or pesticides, and many other materials, but I can still envision them in terms of these basic processes. I'm going to be presenting a basic research tool that you can apply to the flow of anything. When I talk about the flow of a substance, I usually think of beer. So when I talk about a flow, we'll just think about beer and not worry about pesticides or any other chemical.

What is a conceptual model? Now that's hard to describe because we all walk around with conceptual models in our minds; models of the way we envision transports, the world, everything we associate with. We have a concept and it is modeled in our mental processes.

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*Environmental Engineer, Southeast Environmental Research Laboratory

One way we have of communicating this conceptual model is with language. We use words; we write them down; we speak to one another. And as you've seen in this symposium, sometimes our language isn't always the same. I don't mean we speak different dialects or different tongues; I mean we may all speak English and not understand the words. This is exemplified in a short story.

There was a man and a woman who just had a new child. They had to move out of their one-bedroom apartment and so they spent some time looking for a new home. One evening the man came home and said, "I've solved our problem. I bought a condominium." His wife replied, "Good, I can throw away my diagram."

Now I don't advocate throwing away the diagrams, because I think they may be the solution to some of our problems. Diagrams are an explicit, exact method of communicating conceptual ideas, so from here I'll go to the diagrams.

System Diagrams Represent Conceptual Models

What I'm going through now is a series of diagrams. The words on them are not important. The connection of the arrows isn't important. However, the concept of building from a basic block that describes your system (your boundaries in time and space) and then expanding it to the point at which you have a definition you feel is sufficient to handle the problem is important.

In Forrester diagrams of dynamic systems, six symbols are commonly used.

- A solid line represents a directed pathway for transfer of matter or energy.
- A dashed line represents a directed pathway for control or information transfer.
- The cloud symbol represents a source or sink (input or output) outside the defined system boundaries.
- A rectangle indicates storage of matter or energy.
- The valve symbol indicates rates along the associated pathway.
- Finally, the circle represents coefficients and parameters that affect flow rates.

The degree of resolution or complexity of the Forrester diagram of a system may vary considerably depending upon application and resources available for evaluating the hypothesis. While there appears to be no upper limit to the resolution of a model, the lower limit (a single storage component) is demonstrated for a lake in the following example (Figure 1) from O'Melia. The low level of resolution in this example does not necessarily imply that there is a better representation for a particular application.

Figure 1 is Vollenweider's Lake Eutrophication Model. We have an input from some cloud. The clouds indicate sources and sinks that we're not going to be concerned about; they may be important in a particular application, but not in the one that we've described by this diagram. In other words, we're not particularly concerned where it came from; we're just concerned with where it is after it gets here. The rectangle is a body of a lake that's completely described for his purposes by a nutrient concentration. On the right is a flow which is an output. The dotted lines indicate the influence of effects, but not the actual flow of materials.

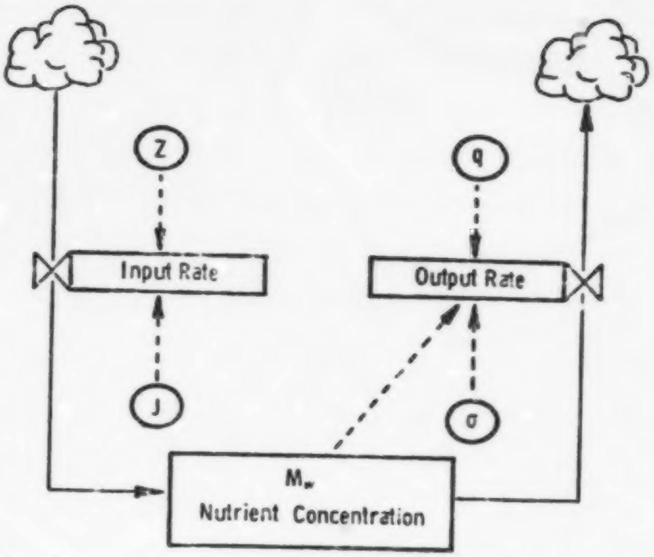
In the next diagram (Figure 2) we take this nutrient content in a lake and say, "That's not very good for our purpose because some of the nutrient is absorbed on particles, some of it is dissolved in the water, and some of it gets soaked up in the biota." Thus we divide up the abiotic component and the biotic component, and we show a lot of interactions between them.

In Figure 3 the biotic concentration of nutrient is coupled to the biomass dynamics. You say, "What's the biotic component?" It's clams in the estuary and they're growing. We want to have them grow, and so their absorption of materials changes.

In Figure 4 we say our body of water is also divided up into areas that have different dynamics and different processes associated with it. In terms of this lake we have a surface layer, epilimnion, hypolimnion, and sediments, each one interacting through settling and wind turbulence and things like that. This is just a rough indication of some of the processes that can affect you here.

Figure 1

Vollenweider Lake Eutrophication Model


Z
q
Input Rate
Output Rate
J
σ
M_w
Nutrient Concentration

$\frac{dM_w}{dt} = \frac{J}{Z} - (\sigma + q)M_w$ where M_w = concentration of nutrient,

J = flux of M to lake,

σ = sedimentation coefficient,

q = flow coefficient, and Z = mean lake depth.

Figure 2

Nutrient Model for Lake with Biotic and Abiotic Storage

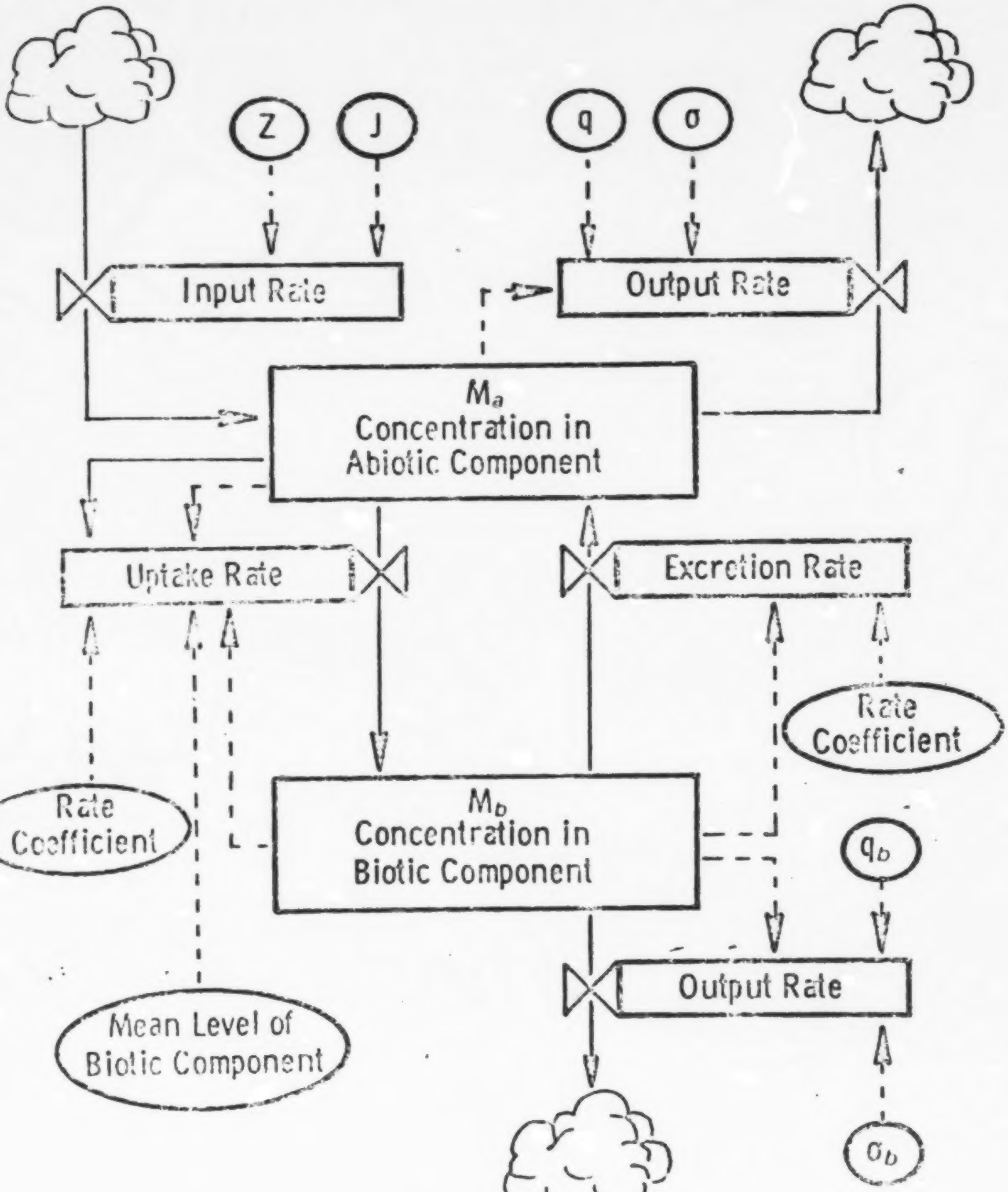

Z
J
q
σ
Input Rate
Output Rate
M_a
Concentration in Abiotic Component
Uptake Rate
Excretion Rate
Rate Coefficient
Rate Coefficient
M_b
Concentration in Biotic Component
q_b
Output Rate
Mean Level of Biotic Component
σ_b

Figure 3

Possible Coupling of Biomass (B) Subsystem with Nutrient Concentration (Mb) Subsystem

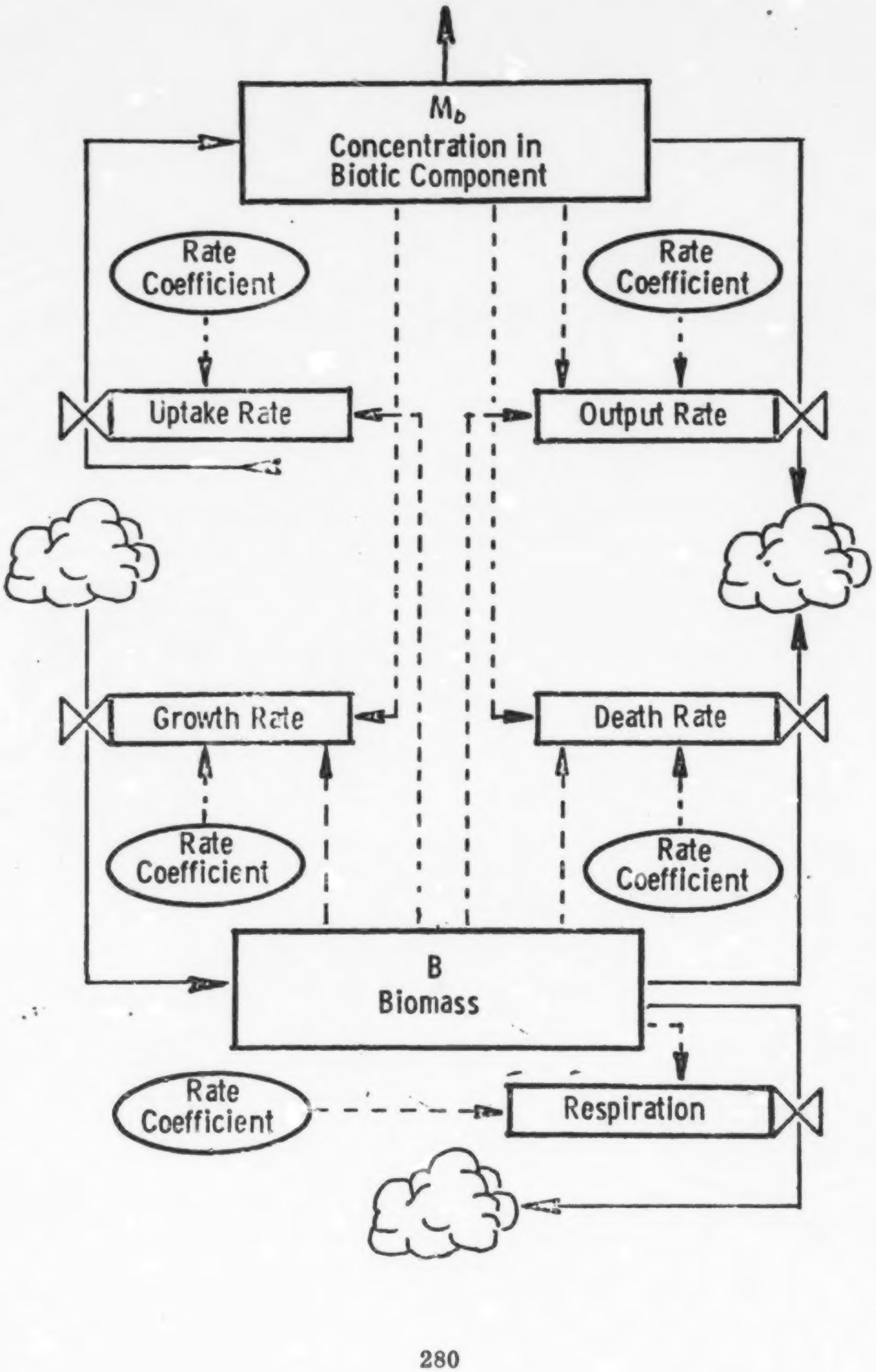
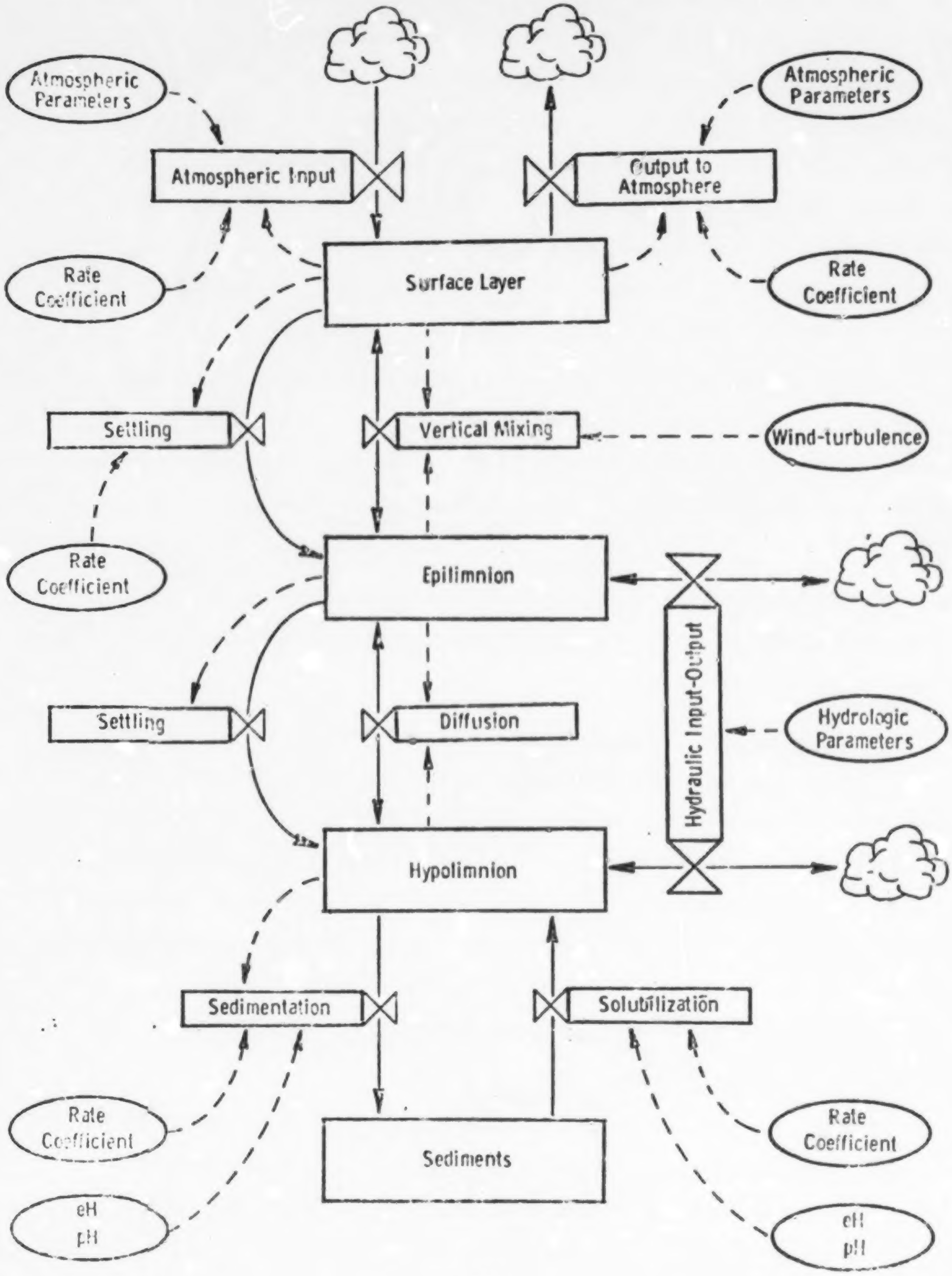

M_b
Concentration in Biotic Component
Rate Coefficient
Rate Coefficient
Uptake Rate
Output Rate
Growth Rate
Death Rate
Rate Coefficient
Rate Coefficient
B
Biomass
Rate Coefficient
Respiration

Figure 4

Vertical Representation of Stratified Lake


Atmospheric Parameters
Atmospheric Parameters
Atmospheric Input
Output to Atmosphere
Rate Coefficient
Surface Layer
Rate Coefficient
Settling
Vertical Mixing
Wind-turbulence
Rate Coefficient
Epilimnion
Settling
Diffusion
Hydraulic Input-Output
Hydrologic Parameters
Hypolimnion
Sedimentation
Solubilization
Rate Coefficient
Sediments
Rate Coefficient
eH
pH
eH
pH

Now, we're going to take the surface layer and in the next diagram (Figure 5) we're going to expand that and show some of the chemical/physical processes that affect the material that was in the surface layer. On the right is the concentration of a pesticide or what have you in the surface layer of the water. This interacts with solar energy because it has a food web, and we have photochemical degradation some place on there, and precipitation input. We've divided the material into inorganic particulates and organic particulates, and it's just a whole bunch of processes that affect the surface layer. Similar processes affect the epilimnion, the the hypolimniun, the sediments, etc.

The next diagram (Figure 6) shows how in the surface food web we can have a similar expansion. We can call them primary producers, consumers, second consumers, and decomposers. This certainly doesn't include all the food web, but at least it includes the primary important parts that give you the essence of your dynamics.

The last diagram (Figure 7) combines all the transports, transformations, and storages previously discussed into one picture. It is overwhelming and so we'll go very quickly to Figure 8.

This is a diagram (Figure 8) taken from an article by Wassily Leontief in Scientific American, and it's demonstrating the structure of the American economy. Now, I don't find this nearly as complicated as that diagram that I just showed you, and yet they have similar information content. You can go from a complicated diagram to this array with columns and rows labeled leather, food and tobacco, lumber and wood, electricity, textiles, etc. The squares in each of the blocks represent the flow of goods or products from, say, apparel and textiles on the left to agriculture on the top. Well the people that work in agriculture have to wear clothes. There's an interaction there.

If you go from those diagrams that I showed you to one of these arrays with squares in them, all of a sudden arrays with squares aren't too hard to understand. The diagrams might have been complicated but the array isn't.

Figure 5

Some of the Storages, Processes, and Subsystems Associated
with the Surface Layer Storage Component

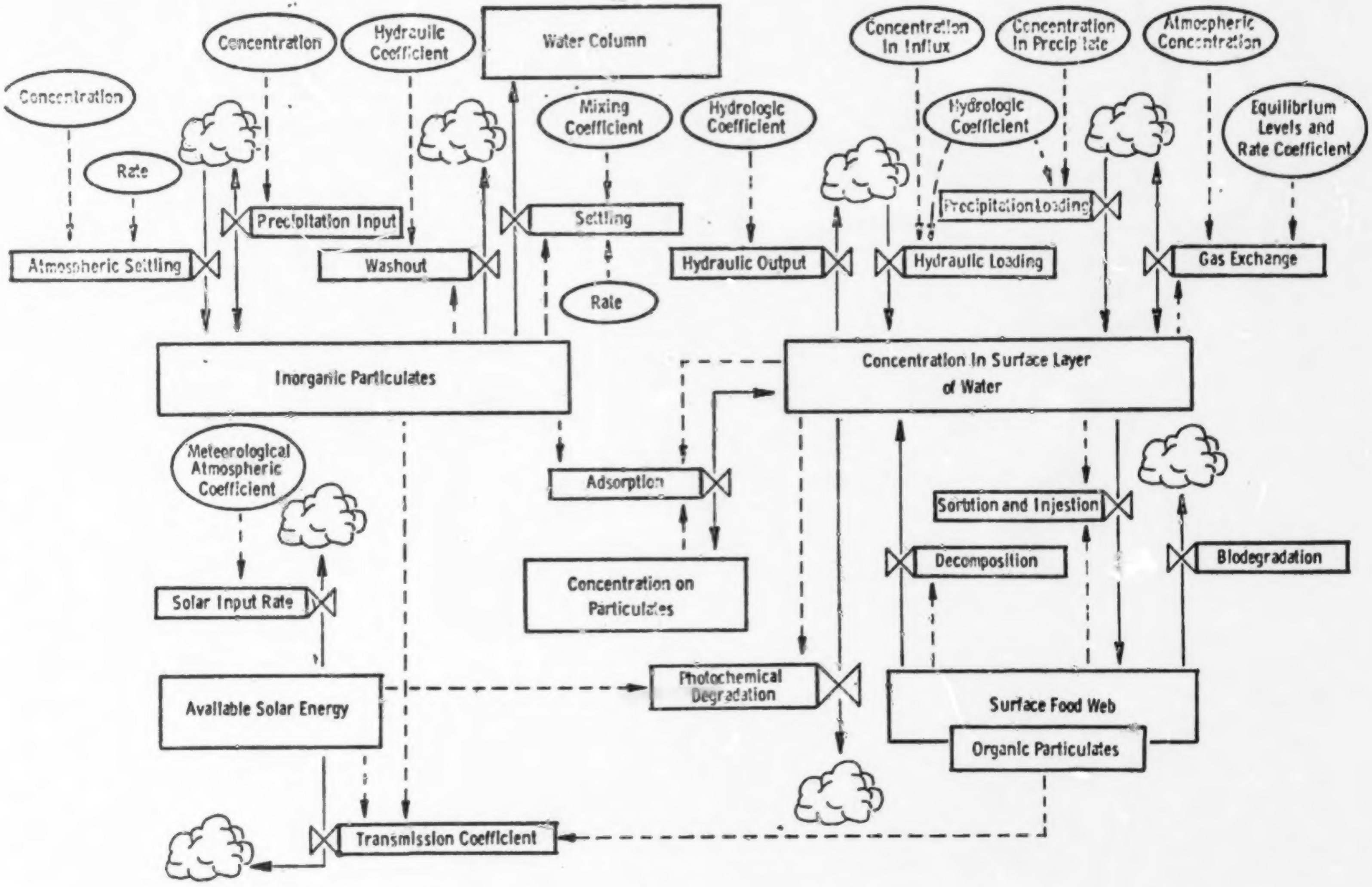

Concentration
Rate
Atmospheric Settling
Concentration
Precipitation Input
Hydraulic Coefficient
Washout
Water Column
Mixing Coefficient
Settling
Rate
Hydrologic Coefficient
Hydraulic Output
Concentration In Influx
Hydrologic Coefficient
Concentration In Precip tate
Precipitation Loading
Hydraulic Loading
Atmospheric Concentration
Equilibrium Levels and Rate Coefficient
Gas Exchange
Inorganic Particulates
Concentration In Surface Layer of Water
Meteorological Atmospheric Coefficient
Solar Input Rate
Adsorption
Concentration on Particulates
Sorbtion and Injestion
Decomposition
Biodegradation
Available Solar Energy
Photochemical Degradation
Surface Food Web
Organic Particulates
Transmission Coefficient

Figure 6

A Skeletal Abstraction of a Food Web

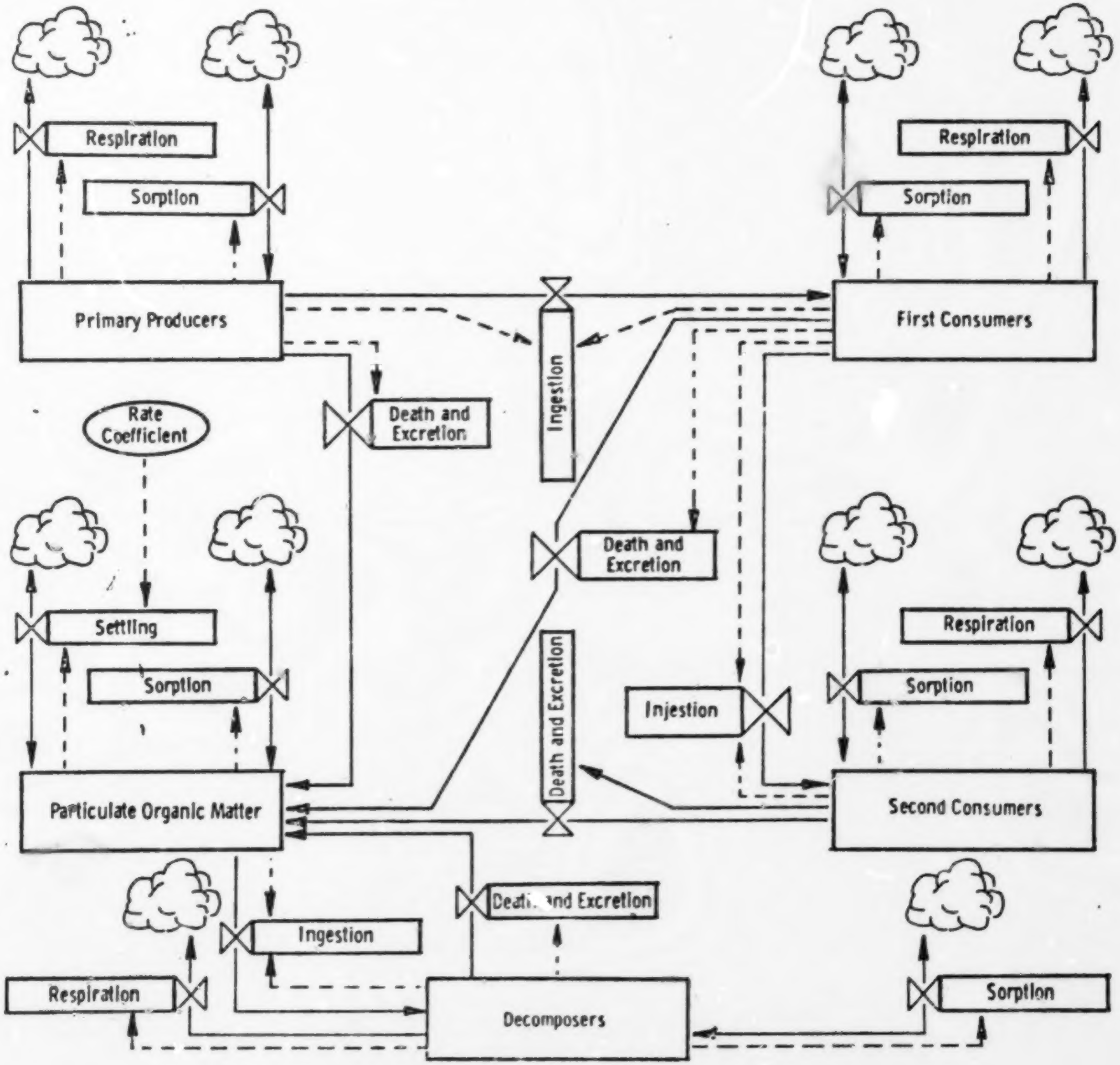

Respiration
Sorption
Primary Producers
Respiration
Sorption
First Consumers
Ingestion
Death and Excretion
Rate Coefficient
Death and Excretion
Settling
Sorption
Particulate Organic Matter
Death and Excretion
Injestion
Respiration
Sorption
Second Consumers
Death and Excretion
Ingestion
Respiration
Decomposers
Sorption

Figure 7

A Minimal Representation for a Pesticide in a Dimictic Lake
(Part 1)

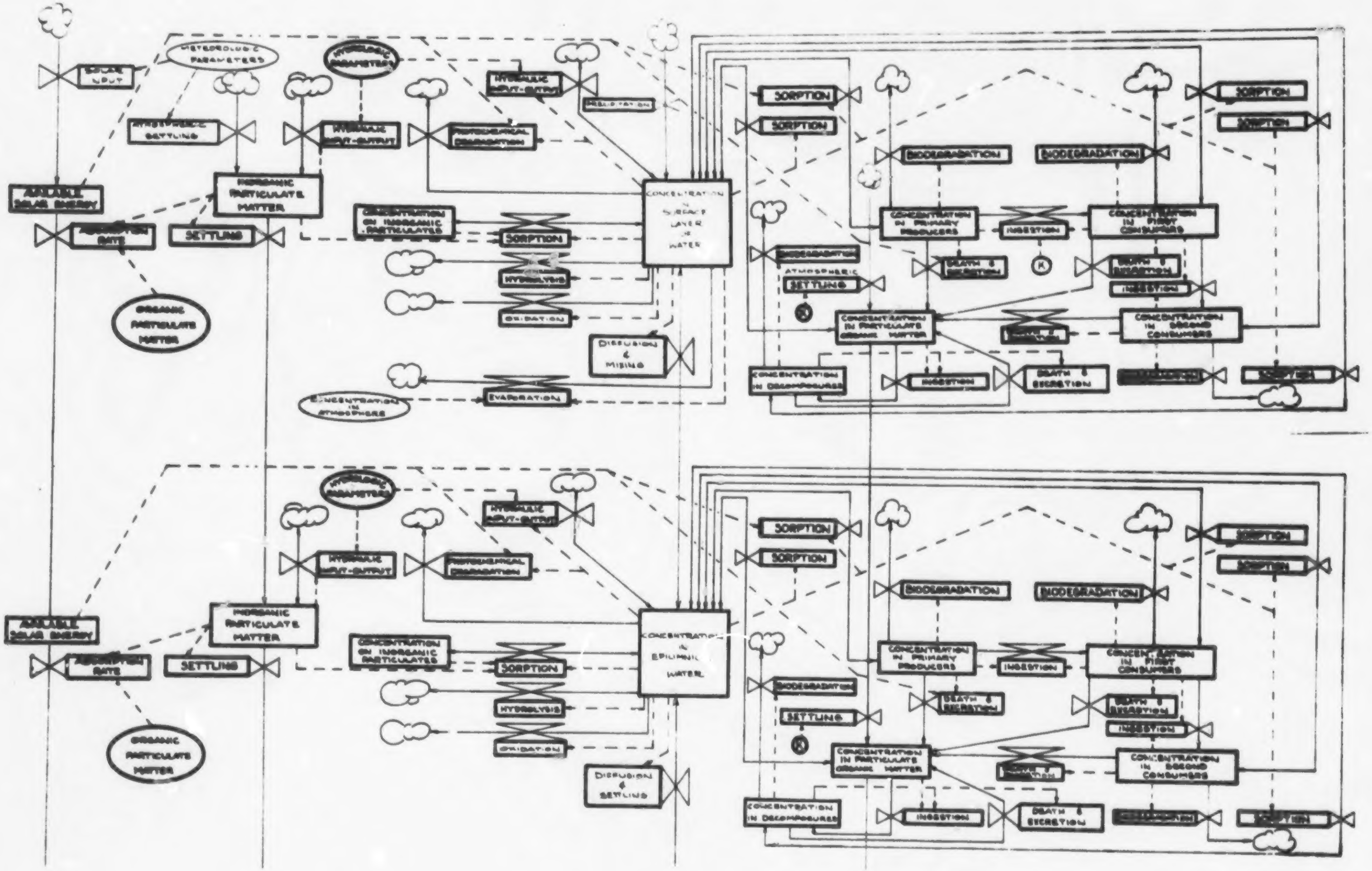

SOLAR INPUT
METEOROLOGIC PARAMETERS
HYDROLOGIC PARAMETERS
ATMOSPHERIC SETTLING
HYDRAULIC INPUT-OUTPUT
PHOTOCHEMICAL DEGRADATION
PRECIPITATION
AVAILABLE SOLAR ENERGY
INORGANIC PARTICULATE MATTER
ABSORPTION RATE
SETTLING
ORGANIC PARTICULATE MATTER
CONCENTRATION ON INORGANIC PARTICULATES
SORPTION
HYDROLYSIS
OXIDATION
CONCENTRATION IN SURFACE LAYER OF WATER
DIFFUSION & MIXING
EVAPORATION
CONCENTRATION IN ATMOSPHERE
SORPTION
SORPTION
BIODEGRADATION
BIODEGRADATION
SORPTION
SORPTION
CONCENTRATION IN PRIMARY PRODUCERS
INGESTION
CONCENTRATION IN FIRST CONSUMERS
BIODEGRADATION
ATMOSPHERIC
SETTLING
DEATH & EXCRETION
K
DEATH & EXCRETION
INGESTION
CONCENTRATION IN PARTICULATE ORGANIC MATTER
CONCENTRATION IN SECOND CONSUMERS
CONCENTRATION IN DECOMPOSERS
INGESTION
DEATH & SECRETION
SORPTION
HYDROLOGIC PARAMETERS
HYDRAULIC INPUT-OUTPUT
HYDRAULIC INPUT-OUTPUT
PHOTOCHEMICAL DEGRADATION
AVAILABLE SOLAR ENERGY
INORGANIC PARTICULATE MATTER
ABSORPTION RATE
SETTLING
ORGANIC PARTICULATE MATTER
CONCENTRATION ON INORGANIC PARTICULATES
SORPTION
HYDROLYSIS
OXIDATION
CONCENTRATION IN EPILIMNIC WATER
DIFFUSION & SETTLING
SORPTION
SORPTION
BIODEGRADATION
BIODEGRADATION
SORPTION
SORPTION
CONCENTRATION IN PRIMARY PRODUCERS
INGESTION
CONCENTRATION IN FIRST CONSUMERS
BIODEGRADATION
SETTLING
DEATH & EXCRETION
DEATH & EXCRETION
INGESTION
CONCENTRATION IN PARTICULATE ORGANIC MATTER
CONCENTRATION IN SECOND CONSUMERS
CONCENTRATION IN DECOMPOSERS
INGESTION
DEATH & SECRETION
SORPTION

Figure 7

A Minimal Representation for a Pesticide in a Dimictic Lake
(Part 2)

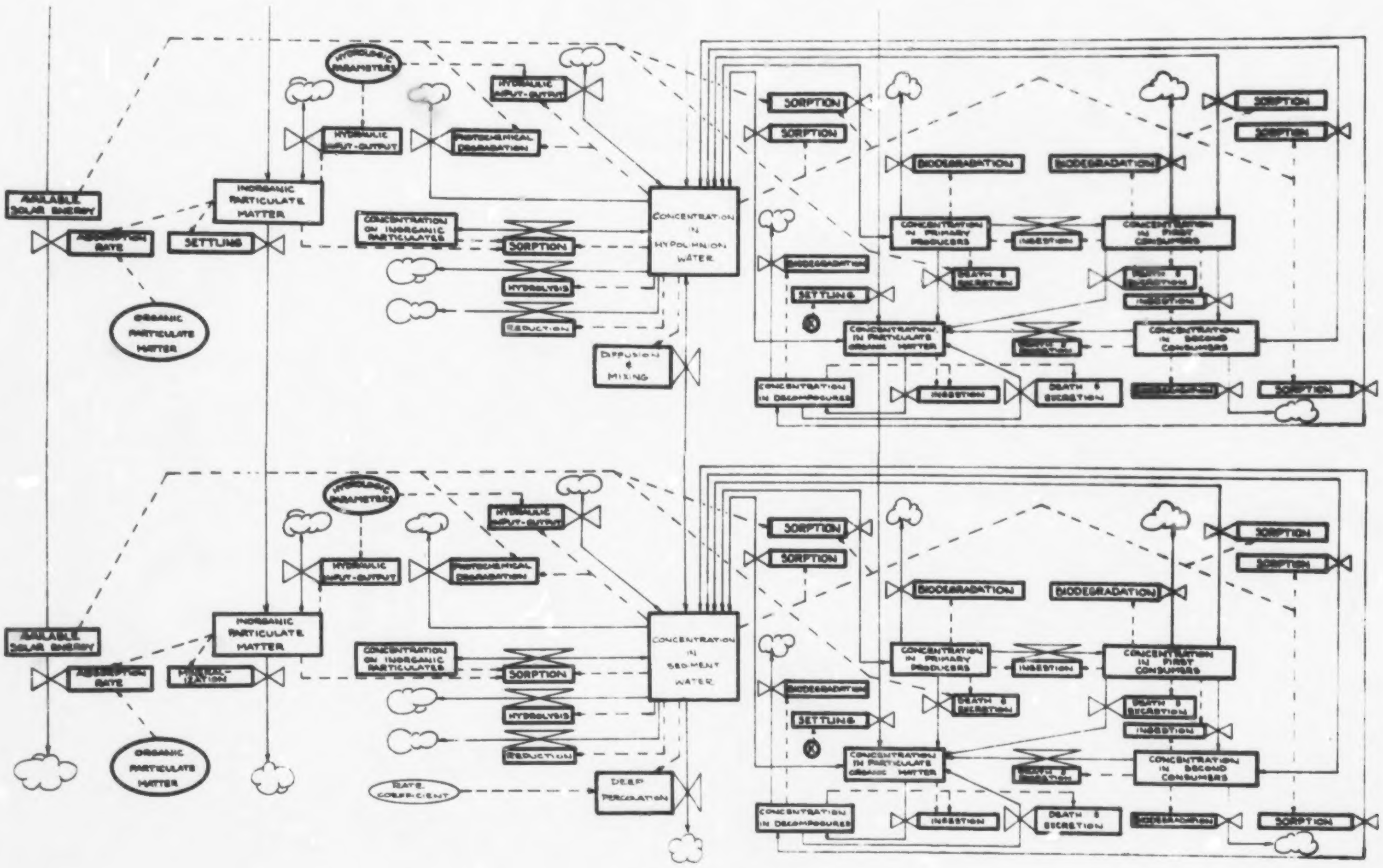
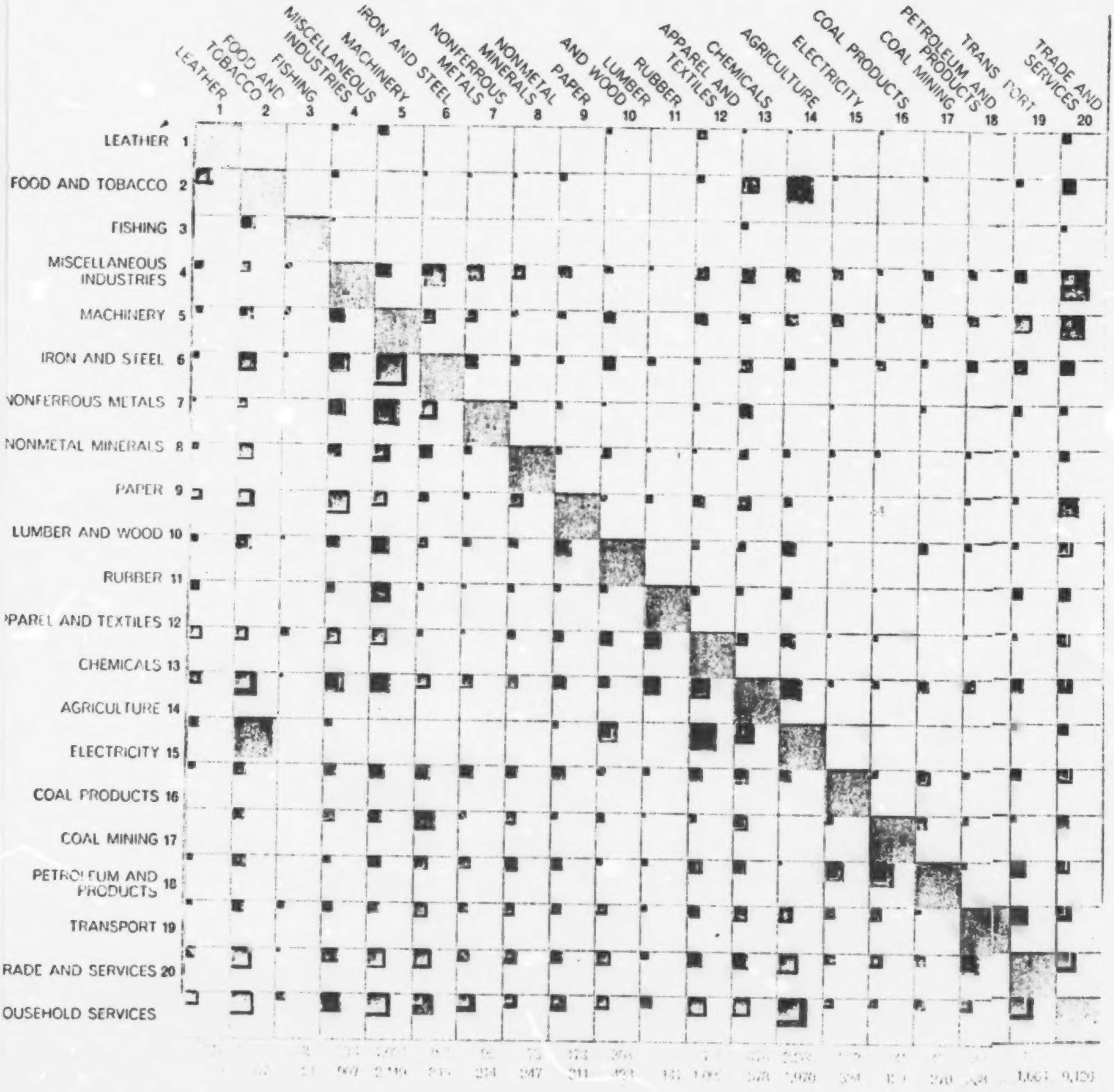

HYDROLOGIC PARAMETERS
HYDRAULIC INPUT-OUTPUT
HYDRAULIC INPUT-OUTPUT
PHOTOCHEMICAL DEGRADATION
AVAILABLE SOLAR ENERGY
INORGANIC PARTICULATE MATTER
ABSORPTION RATE
SETTLING
ORGANIC PARTICULATE MATTER
CONCENTRATION ON INORGANIC PARTICULATES
SORPTION
HYDROLYSIS
REDUCTION
CONCENTRATION IN HYPOLIMNION WATER
DIFFUSION & MIXING
SORPTION
SORPTION
BIODEGRADATION
BIODEGRADATION
SORPTION
SORPTION
CONCENTRATION IN PRIMARY PRODUCERS
INGESTION
CONCENTRATION IN FIRST CONSUMERS
BIODEGRADATION
DEATH & SECRETION
DEATH & SECRETION
SETTLING
INGESTION
CONCENTRATION IN PARTICULATE ORGANIC MATTER
DEATH & SECRETION
CONCENTRATION IN SECOND CONSUMERS
CONCENTRATION IN DECOMPOSERS
INGESTION
DEATH & SECRETION
BIODEGRADATION
SORPTION
HYDROLOGIC PARAMETERS
HYDRAULIC INPUT-OUTPUT
HYDRAULIC INPUT-OUTPUT
PHOTOCHEMICAL DEGRADATION
AVAILABLE SOLAR ENERGY
INORGANIC PARTICULATE MATTER
ABSORPTION RATE
MINERAL-IZATION
ORGANIC PARTICULATE MATTER
CONCENTRATION ON INORGANIC PARTICULATES
SORPTION
HYDROLYSIS
REDUCTION
RATE COEFFICIENT
CONCENTRATION IN SEDIMENT WATER
DEEP PERCOLATION
SORPTION
SORPTION
BIODEGRADATION
BIODEGRADATION
SORPTION
SORPTION
CONCENTRATION IN PRIMARY PRODUCERS
INGESTION
CONCENTRATION IN FIRST CONSUMERS
BIODEGRADATION
DEATH & SECRETION
DEATH & SECRETION
SETTLING
INGESTION
CONCENTRATION IN PARTICULATE ORGANIC MATTER
DEATH & SECRETION
CONCENTRATION IN SECOND CONSUMERS
CONCENTRATION IN DECOMPOSERS
INGESTION
DEATH & SECRETION
BIODEGRADATION
SORPTION

Figure 8

Developed Economics*



*From Leontief, W. "The Structure of Development." Scientific American September 1963.

Now, if you'll let me call that array with all the boxes in it a matrix, I'm into mathematics and we don't have to worry about the diagrams. We can throw the diagrams out now! The idea that I'm trying to get to very strongly is (1) we all have these conceptual models, (2) we can put them into simple diagrams, (3) we can make the diagrams more complicated, (4) we can take the complicated diagram and turn it into a matrix, and (5) we can go to linear or matrix algebra and make some statements, some logically strong statements. These statements are dependent upon the assumptions you made when you drew your first diagram and all the assumptions along the way.

The rest of my talk is concerned with the type of statements that you can make as a tool for preliminary design of a research program. You have a problem with the flow of any substance; for example, beer from the Mississippi River into an estuary, and you want to handle the first approach — nobody's ever looked at beer in the Mississippi flowing into the estuary. You need to know (1) what to measure, (2) how often to measure it, and (3) how precise and accurate your measurements have to be.

Preliminary Analysis Techniques for Linear System Approximations

If we take an array similar to that of Figure 8 which represents a complicated diagram and replace the shaded squares in the grid by numbers which are equal to their area, then we have a matrix which represents a first order approximation of a mathematical model of the original concept. This matrix, call it "A," has numerous properties which can be investigated mathematically and then translated into statements about the system under study. These statements are approximate and as such cannot tell us all about the system. However, they can help us to ask the right questions of the system in a research program.

What do you measure? Some of the interaction coefficients, the values in the A matrix, may be determined by analysis of the inputs and outputs of the system using a technique called component analysis. Thus if we know the input of beer to the Mississippi and the output of beer from the Mississippi, then component analysis can tell us if it is possible to determine the rate of storage of beer in the sediments of the river without direct measurement of the storage. So from the component analysis on your preliminary description of your system, you can say, "What do I have to measure and what can I find out cheaply by just measuring the input and the output and plugging that in the machine?"

The array of Figure 8 from Wassily Leontief is related to economic input/output analysis, which has been introduced into ecology by Bruce Hannon in a recent article in the Journal of Theoretical Biology. This flow analysis gives you a measure at steady state (i.e., when things have settled down with a given input) of the amount of flow between one storage compartment in your model and another. If a flow is really small and the interaction with the system is small, then that's one you may not want to spend too much money on measuring. You'll go for the big flows as they're predicted by your model, and then you can go check that in the field and revamp your model and work it around again.

How often do you measure these things? Well, a group of graduate students at the University of Georgia and Hank Shugart, who's with the Oak Ridge people now, have shown that an ecosystem's frequency response is very accurately described by a second order system approximation. This means that you can take two blocks in your model and lump your whole ecosystem into them with respect to the frequency response analysis. In other words, if you ask how fast things are going to change when you change the input of beer to the Mississippi River, then that frequency response is reasonably dependent on a second order approximation.

You make a second order approximation based on the matrix and this gives you back what we call an undamped natural frequency. This natural frequency is related to how fast your ecosystem, your system whatever it may be, is going to change, and that gives you an approximation of how often you want to measure what it is you have to measure on the system.

Finally, with respect to accuracy and precision of the measurements, there's a sensitivity analysis. This analysis can tell you how much effect on some measure of total system behavior a small change in any one of those coefficients represented in the A matrix or on your diagram is going to have. In other words, if the input of beer at St. Louis is very large, but a change in it of one glass more or less is going to really affect the clam production in the estuary, then you'd better be very accurate in your measurement of that beer. Even though the number may be very large, you're going to have to know a small deviation. If way upstream the input may be small and changes that are double and tripling aren't going to have much effect based on sensitivity analysis, then you can use a very coarse measurement or maybe even ignore the measurement completely.

All of those analytical techniques are available right now and they're very straightforward. There's one more that I'd like to talk about which I call topological analysis.

The actual behavior of a system as represented by the diagram depends on four things — the inputs to that diagram or to the system itself, the coefficients, the topology that you hypothesize (in other words, is the leg bone connected to the neckbone) and the structure which includes how the rates flow through that topology to influence other rates (e.g., how does diethylstibesterol affect emphysema in California?) So with respect to those four levels of analysis deals only with whether you hypothesize that the leg bone is in effect connected to the neck bone and you leave out the rest of the body.

This analysis I hope is going to be available within a year's time, and it will turn out to be quite useful in a very real aspect. We talk about going from the test tube to the field, from the laboratory to the ecosystem, and this topological analysis is one measure of what you gain or lose when you do that.

If you hypothesize in your representation that grasses, a field crop, can uptake beer and affect mice that's one thing. If you hypothesize that grasses are divided up among seeds, stems, leaves and roots, and each of these individually with different rates of beer transport affect mice (e.g., the mice absorb more beer from the seeds than they do from the roots because of their feeding habits), then what do you lose when you lump all the grasses into grass without paying attention to the seeds, stems, leaves, and roots and their separate interactions? Simplicity is gained but there are many things which you may lose. Most of them might be referred to as richness of behavior. Topological analysis provides one of the measures of richness of behavior.

Now if you combine all five of these analytic techniques and use them as a cheap linear approximation, a first step toward looking at something that you're not used to looking at or toward looking at something which you have always looked at with a mind toward describing instead of analyzing, then it may give you a good way to save some money in your research program. That's what I'm advocating.

Summary of Preliminary Analyses

Topological analysis is currently being developed by a group of Dr. B.C. Patten's graduate students at the University of Georgia. This technique is intended to allow determination of the influence of the topological structure on system behavior. Such information is useful in evaluating alternative system structures and particularly in determining the effects of reduction or aggregation of components.

Flow analysis or input-output analysis is based upon the manipulation of the A coefficient matrix in the linear, donor-control approximation. Briefly, a matrix, G, is generated by

$$G = \sum_{i=1}^{\infty} A^i$$

in which each element, G_{ij}, is a relative measure of the fraction of flow out of storage j that appears as input to storage i under steady state conditions. This information may be used to identify important processes or flow paths in the system.

Sensitivity analysis may be used to evaluate the effect of a parameter perturbation, v(t), upon the storage levels in the system. The measure of sensitivity, S, is useful in determining which parameters have a prominent effect upon system behavior. A linear approximation of S(t) is determined from

$$\frac{d\,S(t)}{dt} \approx \left[\frac{\partial\left(\frac{dX_i}{dt}\right)}{\partial\, X_j}\right] S(t) + \left[\frac{\partial\left(\frac{dX_i}{dt}\right)}{\partial\, A_{ij}}\right] v(t)$$

where the terms in brackets are Jacobian matrixes. With a unit perturbation of each parameter, A_{ij}, the steady state values of S for each storage variable may be used as a relative measure of system sensitivity to each parameter.

Frequency response analysis provides frequency related measures of system behavior. Both the referenced papers and current studies indicate that the damping ratio (ζ) and the undamped natural frequency (ω_n) are well described by a second-order control system approximation of the system. When the system is overdamped (most ecosystems appear to be so), then the undamped natural frequency becomes a measure of the maximum required sampling rate for system variables.

Component analysis allows numerical determination of a limited number of coefficient values from the A matrix of the linear, donor-controlled representation and the system transfer function as determined from experimental input-output data.

Topological analysis can be used as an aid in evaluating the influence of connectivity upon process rates in the system. Flow analysis can provide a measure of steady state distribution of flow through the process pathways. A preliminary sensitivity analysis can determine the effect of an error in parameter estimation upon storage levels and hence upon flows. These three evaluations of process-system interaction provide criteria for elimination of components that have the least effect on system behavior, thus systematically reducing the graphic representation.

These analyses may be applied to a mathematical approximation of the reduced representation. This results in information that may be used as a first approximation in choosing measurement methods and sampling rates for evaluation of system hypotheses.

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DR. BUCKLEY: I would suggest that this is an appropriate time for questions, and again I'd like to sit down and leave the question answering to Dr. Glass and his colleagues. I'd make only one observation first, and it stems directly from the last presentation. And it is something that concerns me and I'm sure it concerns all of you here — how do you put the bits and pieces of information that we have together? How do you interpret the significance of the different odd facts, sometimes pleasant and sometimes unpleasant, and how do you deal with the question of their significance, how do you deal with things as a whole?

And I can assure you we don't have all the answers, but we surely are interested in pursuing this, and I do think that the aggregate of what we've just heard is aimed in that direction.

DR. NORMAN GLASS: I think it's obvious from these presentations too that this is a new program, which will have far more output in the near and distant future than it's had in the last few months, but I think it's also clear that we're trying to adopt a more or less holistic, integrated type of program. I'd like to invite any questions you might have at this time, addressed to anybody on the panel.

MR. ALFRED MITLEHNER: I suppose this question goes to Dr. Axelrod as much as anyone else, and that is in view of the very preliminary nature of the information discussed and presented here this morning, how does Dr. Axelrod view this information with regard to the establishment of criteria for the classification of pesticides? More specifically, are we really ready to establish specific criteria that would relate to the classification of pesticides?

DR. AXELROD: It's a multifaceted question, and I think I can answer you best by congratulating Mr. Hill on a genuinely new black-box look at some of the problems that we in the Agency must address ourselves to now and in the future. I'm not too much on models, and particularly mathematical models in the past, but I think the approach of systems analysis, the engineering approach, and almost bilogically cybernetic approach introduced here this morning by Mr. Hill and his colleagues may eventually solve some differential equations simultaneously. Approaches such as Dr. Cooper from Michigan State has taken in the area of ecology, where one pinpoints the input/output from the black box as a systems analysis and the major thrust becomes one of understanding exactly what makes that ecological system run, is the type of research which will in the final analysis answer what in science might be considered mundane questions, but which are paramount to a regulatory agency.

Many millions of dollars are spent in litigations, in argumentations, and adversary approaches. Very little of those arguments are based on sound, predictive concepts, and it's not just for this Agency, but it is for the benefit of agriculture and the industrial sector which addresses itself to the agricultural community that we have intelligent data inputs of predictive value for solving problems before they become adversary problems.

The adversary is the last final common denominator of ignorance, and the solutions there become ones of judgmental values and legal matters, but not of science. I think that relationship between the type of — and I say this very much in a double quote — blue sky that Mr. Hill approaches, or Dr. Cooper, or people of his abilities, is one which impacts directly on the ability to solve problems and issues including the classification problems in the future. You cannot solve problems today based on a meager information feedback system. You have to plan for the future, and your inputs financially, resource-wise and manpower and brainpower-wise, are the only answers to intelligent future decision-making and policy-making.

There is a real paucity in the data banks of knowledge. There's only a few days' worth of corn left out there; there's only a few hours left in the ability to predict on a scientific basis many of the problems and issues that are involved in this Agency. And I think that the dollars and resources we put into the type of work that these people enunciated up here, and particularly for a base line of what Mr. Hill is doing, will serve a great purpose in resource conservation in the courtroom later on, when we can have data bases to predict from values on a statistical basis.

MR. CHARLES KRISTER: Can we get back to the real world? If Dr. Korp is not here, I'll direct this to Mr. Hill.

Can we direct our attention to the microcosm that's very important to industry. Has any thought been given to making a study of the ecosystem in the Pesticides Regulation Division?

I would hope that the Pesticide Division would be one of the first systems to be studied and, again, to find out what the important factors are that should be involved in the input — get into that black box that some of us have been in quite a while.

DR. BUCKLEY: I'd take that as a comment and not as a question, Chris. That may be a good time for us to go have a cup of coffee. There will be opportunity for questions later, and before we do break this up I do wish to thank my colleagues for a fine presentation this morning.

DR. BUCKLEY: I would like to introduce now the second half of this morning's program. Until now we have talked about ecological and environmental considerations, but I assure you that in my view of the world, man fits in those models that Jim Hill was talking about.

To make one point before we go on to health, I don't know whether it's entirely clear or not, but the people who sat here this morning in the earlier part of this program are geographically located in different places. The point that I want to make is that they talk together and they know one another. We have a single program which in a sense is tied together in the generation and interpretation of data to be used in a conceptual way such as that that was described by the very last speaker. Mr. Hill. I didn't want anyone to get the impression that everything is all in one place.

The other point I want to make is that we feel no compulsion to be the generators of all data. In fact, as this progresses and the development of understanding and interpreation goes on, we would like to feel free to call on all of you, those of you in other Federal agencies, those of you in academia, and especially those of you in industry, to help us not only with the data that you may already have provided in some fashion or another to the Federal government, but also with new data which we can use in this way.

We'd like to be completely open in exchange of views and in telling you why we want information and how we're going to use it. We've tried to tell you with this conceptual model what we're up to. The boiled down version of this is that we want to understand what's happening.

I feel one further need to make sure that you understand that I am in the research end of the business, and my colleagues who were and are now on the platform are in the research end of the business. I want to draw a very clean and neat distinction between what research and researchers do and other activities.

It seems to me very clear that research must provide the scientific basis on which decisions can be based. It owes an evaluation of what risks or hazards may take place under a given set of circumstances. It owes this in as explicit a fashion as it can make, and it owes this to the people who do make decisions. It also owes an obligation to refrain in the presentation of such data from implying an action that should follow.

In summing this up, it's a summation of what's known and a summation of what's not. An indication of what gaps there are, but refraining from saying "research must be carried out to fill these gaps." I think that's an entirely different issue. There may be other gaps in other fields that are more important in a priority way, and I think that's an administrative decision, wholly separable from the research process. I'm trying to express to you a set of feelings that I personally hold very deeply, that I hope will be reflected more and more in the documents that the Environmental Protection Agency produces as scientific background documents.

We expect to spend some days next week with another set of people talking about this very topic, and this I think is something that with great good fortune we will find more and more the case in background documents across all areas in the environment — not just those concerned with pesticides. This is a gratuitous lecture, not on the schedule, but nonetheless one that I feel our stock in trade is dependent upon — being able to unemotionally and as clearly as possible express what will happen, and, equally, to refrain from the conclusion that this should or should not happen. That's not our business as researchers.

Now I may in fact put on a different hat, and at the time that I put that on, I feel entitled to one vote along with others as to what the Agency may do with the information. It is important to distinguish between what I know as a researcher and what I believe or prefer as an individual member of society.

Now with this set of gratuitous comments out of the way, I'd like to turn to the human health aspects part of the program.

INTRA- AND EXTRAMURAL HEALTH EFFECTS RESEARCH

Ronald F. Baron, Ph. D. *

I handed out a little brochure called Intramural and Extramural Health Effects Research, and I'd like to call your attention to a couple of things. The first page relates to this Alternative (Substitute) Chemicals Program. This whole listing of tasks, of areas of interest to our laboratory, is our FY '75 program plans. The first page is what we are going to be doing in this program. The next few pages relate to other ongoing programs within our laboratory in health effects and chemistry. I must point out that we have combined both health effects and chemistry.

I would also like to point up another document which may be of value to some people, the EXPRO-75. This is our extramural program for '75. I don't want to go into detail with regard to our extramural and intramural programs. I would like to point out with regard to these plans — most of them not fully implemented, some of them not even fully planned — that these are areas of research in which we are going to work.

With regard to EXPRO-75 and the brochure I'll be very glad to answer questions with regard to the Substitute Chemicals Program at this time. Any questions relating to any other areas of research in that document should be presented at some later time, either here or in Research Triangle Park, North Carolina.

This discussion will center around the scope of work and the ultimate goals as observed in 1974, what we have accomplished and how, and what we will do in our health effects program at Research Triangle Park.

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*Physical Science Administrator, National Environmental Research Center

At this point, I would like to diverge from this planned discussion of our Alternative Chemicals Program to comment on a very specific question or a series of questions has been raised relating to pesticides used for research in this program.

Questions have been raised as to the quantity, quality, and sources of material which were originally designated as compounds of interest, substitute chemicals, alternate chemicals. Approximately 6 months ago a decision was made to obtain a quantity of material to be used in the entire research program when applicable, to maintain uniformity at least in the material being used.

This effort is a throwback from several years of experience in Food and Drug and from what I have heard of happenings in USDA in which research performed over a period of several years was never fully substantiated because of the lack of quality control of the chemical used. Thus, as I mentioned, a decision was made to obtain a sample of material, either through industry cooperation or through the purchase of single or multiple large batch lots, and to store the samples in a single repository to be disseminated as needed.

Within the framework of the chemical contaminants program, we are maintaining a repository in which pesticides are to be stored under the conditions which would allow maximum storage with consideration of the conditions of safety and stability of the product. In all instances it was determined that the majority of sample material would be stored in bulk at sub-freezing temperatures in an inert atmosphere and the samples to be sent out would be repackaged into smaller quantities of approximately one pound, one pint, or less and would be stored in desiccators at sub-freezing temperatures. An attempt would be made to obtain a 100-pound or 50-kilogram sample of material. Now I know this has raised many, many questions and I'll attempt to resolve some of them.

This quantity of material that was requested was not evaluated on the basis of any individual pesticide nor on the basis of the toxicology of any single pesticide or even any group of pesticides. The request for 50 kilograms had nothing to do with any individual compound, but was made only on the basis of the overall general program. The only consideration was that a sufficient quantity of sample should be available for a potentially 4- or 5-year program to allow adequate quantities of research in all areas that we can at this particular point anticipate.

In particular, a large quantity of sample was thought to be necessary with regard to one particular program. It was thought to be necessary for a potential chemical contaminants program, which I'm going to go into in a few minutes.

We had decided that we would be interested in a chemical contaminants program in which a level of 0.05 percent of a technical mixture of material would be of interest to us. What the interest is is debatable at this particular point. We may be interested in the toxicology; we may be interested in the chemistry. But at any rate we decided at this particular point several months ago that a contaminant present at the level of .05 percent would be of interest.

I did some quick calculations and found that if we wanted to obtain this contaminant material which would be present at .05 percent, 100 pounds of material would yield a sample of about 25 grams of this contaminant. Now this means if we were to take this whole 100-pound lot and were to extract it and were very good at purifying, we could get out a sample of 25 grams.

This is wholly illogical. We're not anticipating this, but if it was necessary to obtain a very, very small impurity that was very, very significant and we needed a 25-gram sample for chemical evaluation or toxicology or long-term feeding studies, our 100-pound sample would yield us only 25 grams. I want to point out that this goal of isolating a contaminant from this vast quantity is one that we never expected to reach, but we want you to know that we considered it.

I'd like to point out that we did not fully take into consideration the toxicology of the individual pesticide when requesting a 100-pound sample. A sample of 100 pounds of material such as Temik or aldicarb would certainly not fall into the same category as a 100-pound sample of material such as atrazine or captan. Thus, we must be faulted, and I'll take full responsibility for not considering all aspects and especially the toxicological aspects when we brought up this idea of 100 pounds. In most instances a 5- to 25-poound sample would be more than sufficient for all of our studies.

A consideration was made of the source of material for the study. In the chemical contaminants program, sufficient funds were provided for the purchase over the counter of sufficient quantities of material to allow us to continue the program as I have specified.

However, an attempt is currently being made to obtain, through the cooperation of industry, the necessary pesticides in an effort to allow industry to be a part of this program, to maintain its own source of reference material for the program, and if necessary to question and discuss any results on the basis of their own studies with their own compounds.

I think it would be rather difficult to fully accept the consequence of using material purchased outside of the currently available manufacturing sources, as too many things can happen to a sample after it has left the manufacturing plant. I would like to point out that the product we were interested in obtaining for this study is a technical product, and we would like the material that is available at "the end of the stream of manufacturing."

In no instance, even though we asked for a technical product, would we be interested in disrupting the manufacturing process to obtain a sampling of material prior to its final removal from the factory. In short we are interested in the material as it leaves the plant for shipment and becomes available for the formulators and subsequent handling.

In some instances it was pointed out that a technical product is not available but a formulated or semiformulated product might be available, and I wish to point out again that if this is the product that leaves the plant, this is the product in which we are interested. If a pesticide is manufactured as a technical product and is formulated or partially formulated in one operation, then this is the product we would like to use. I wish to emphasize that we do not and did not wish to interrupt the technical production of pesticides to obtain a sample for our research.

It has been suggested that we should obtain for this activity a sample consisting of mixtures of several batch lots to assure reproducibility of the manufacturing system. It has also been suggested that since there may be several manufacturers of a known product, we would want to use several manufacturing products for our studies. We further questioned the choice of material wanted for this study with regard to whether we were to use a technical or actually formulated material and what we were going to do about the toxicity of diluents in our program.

We considered these points and decided that we would use a single technical material, so that if there was a problem we might be able to identify it immediately. By this I mean we would not want to take a sample from several different manufacturers or from several different manufacturing runs within the processing plant and lump them together.

We decided that we were going to attempt to determine if there were differences in products of several manufacturers. We were and are able to obtain samples of such materials. These are the same or similar materials produced by different manufacturers. As pointed out a little while ago with regard to the repository and storage of materials, we attempted to devise a system in which minimum problems in storage and maintenance of the material would be encountered. The material is to be stored at sub-zero temperatures in an inert atmosphere in an attempt to maintain the material for a period of 4 to 5 years.

In addition, it is anticipated that industry would maintain a similar sample of the material, and any questions raised on the integrity of the material would thus be verifiable. Now just this morning one of our colleagues here raised another point which I hadn't considered: What do we do at the end of the program when we've got 95 pounds of material left over? Would we send it back for their disposal or how would we handle it?

I have to admit we have not fielded all the questions, and I'm very grateful that we've had this opportunity to get together and have some of these raised. At this point I can't answer the question of what would happen if we had 95 pounds of a material that's very toxic left over in our repository. If the energy crisis continues, I think we'll know what to do with it, but I really don't know at this particular point. We would probably request a little bit of help in disposal.

These are some of the questions that we have considered with regard to this request of a sample of 100 pounds of material which has raised many, many eyebrows. I would like to ask if there are any more questions, or if there are any more feelings about this I'd like to try to respond to them. But right now I'd like to go into the direct aspects of the program. My primary purpose and mission is to give you a little background and information as to what we have done with regard to the program up to this point.

I've broken this program into two areas, toxicology and chemistry, and as I said before they are so interrelated it's going to be difficult to disconnect them. A program is underway right now within the framework of what we call chemistry for the optimization and full evaluation of a GLC detector, the Hall-Tracor Detector, for the sensitive detection of nitrogen, halogen, and sulfur-containing pesticides.

This detector is being evaluated for use in the analysis of pesticide residues in environmental samples. At present the microelectrolytic conductivity detector as generated by Dr. Hall from Purdue University has been shown to be sensitive and selective to halogen, nitrogen, and sulfur-containing materials and approaches the electron capture detection in sensitivity.

The detector does not respond to most of the substances that interfere with EC detection and has a wide linear range. When fully optimized the detector will be of value to all researchers in the field of pesticides and contaminants. It will provide not only a much needed sensitivity and a confirmatory technique, but might even replace the electron capture for routine determinations.

Studies are currently in progress to optimize and evaluate the detector for selective sub-nanogram sensitivity to sulfur-containing pesticides and their metabolites, as well as for the determination of chlorinated materials. The studies will attempt to demonstrate the usefulness of the detector for differentiating chlorinated pesticides, polychlorinated biphenyls, polychlorinated napthalenes, and low levels of other materials. In addition, work will be performed in the area of response, reliability, and ease of operation of this particular detector.

Another area of interest is the extension of currently available clean-up procedures to include pesticides not generally included in a multiresidue detection system. These materials might be the materials which are substitutes for deregistered pesticides.

In addition an effort will be made to integrate liquid chromatography as a clean-up and separation procedure for the multiresidue detection system. Initially, methodology must be developed for pesticides which do not fit into accepted schemes of multiresidue methodology. Alternations of known methods such as the Mills procedure or the Shafik procedure will most likely result in acceptable recoveries for pesticides not presently included in existing schemes.

The introduction of liquid chromatography may provide analytical chemistry with a technique for the routine determination of very hard to evaluate chemicals. Two other areas of interest include the identification of toxic impurities in technical grade material and toxicological evaluation of materials found to be impurities of interest.

This latter toxicological area is addressing itself to the idea of fulfilling toxicity screening and testing procedures necessary to provide data to fill out the data base as specified within the framework of the OPP review program. This effort will provide capability for oral, dermal, and inhalation exposure to small mammals; it will provide the toxicology input following review procedures to fill out the data base.

The scope of this work is divided into two main areas. The first one, probably the most important one, is to respond to inquiries for data from the ongoing review process, and this is to respond immediately to inquiries. The second is to respond to inquiries for data on compounds derived from the studies on the characterization of impurities of interest in the technical formulation.

It had been anticipated that several compounds would be reviewed over the first year and that data would be missing in the toxicological evaluation. These data would be requested and ultimately the Pesticide and Toxic Substances Effects Laboratory would provide a rapid turn-around time in the response to these inquiries.

The chemical contaminants program consists of several parts. One, as mentioned before, we will maintain a repository for all pesticides to be used in the study by all researchers.

Two, a theoretical organic chemistry paper evaluation. This is a paper and pencil evaluation of the manufacturing process used by the industry for pesticides of interest. As suggested by the patent and open literature, an evaluation is to be made of the synthesis route. An effort will be made to determine whether toxic impurities are present or can be formed within the framework of the synthetic routes being followed or the ones that we know about.

It is anticipated as evidenced on the basis of dioxins and benzofurans produced in the synthesis of chlorinated aromatic compounds that the possibility exists for a number of impurities. It has been considered that in the preparation of such materials as parathion, the reaction of dimethylthiophosphorochloridate might result in TEPP. Without anticipating that revelations such as this would be of any major consequence, it is reassuring to believe that this would be the only contaminant that could be expected under a particular synthesis procedure.

It is anticipated that in this paper exercise, the industry might cooperate with EPA in allowing the conditions to be known under which the compounds were actually synthesized. If such information concerning synthetic routes is not forthcoming, then all information would be reviewed from the patent and open literature.

Trade secrets — and I believe this is an area that one might consider to be a trade secret — in the evaluation of the synthesis of a product will be maintained at all times. On the pesticides to be used in this program we will do a preliminary analysis which is predominantly a GC assay followed by mass spec and a computer analysis to determine on a "rough and dirty scale" the impurities in an analytical mixture.

This preliminary screening will be followed, if deemed necessary by the background information we have obtained by the paper synthesis evaluation route or even by our own quick and dirty method, by other techniques for the isolation or characterization of impurities. At this particular point possible attendant toxicological studies would be considered.

The objectives of this particular program are to chemically identify impurities and contaminants in the technical mixtures which may present problems and if necessary to evaluate the toxicological significance of the impurities.

It is estimated in this work that many synthetic routes would be evaluated. It is also estimated that there may be a small number of compounds that would be evaluated that may have to go into further detailed chemical analysis to elucidate their structure. I want to point out, as I said, that all compounds that we are going to use in this particular structure are going to be evaluated on the quick and dirty analysis. Some of this information is available and may be made available to us.

We will, however, run through all the compounds quickly. There will be very few compounds which will have to be studied on a large scale. I want to emphasize — and I've heard this word used — I want to emphasize that this particular program is not in effect a "witch-hunt" for pesticide impurities that will destroy or raise questions on the efficacy of the compound for use in agriculture.

Rather, it is the sole aim and goal of this testing procedure to prevent or attempt to prevent with hindsight, the occurrence of another tetrachlorodibenzodioxin contaminant program as we all know originated with 2,4,5-T.

The last and major thrust of PTSEL's program is to provide information on the inhalation toxicology of pesticides. I would like to point out at this time that the research aims of our program are two-fold. One, primarily to respond to questions raised within the framework of the review function to fill out a data base, and two, to perform research in areas of known deficiencies in which toxicological information would be of value in the overall assessment. In this instance it was defined that inhalation toxicology is an area in which data are not available in most instances and certain data would be of value in an evaluation of a pesticide.

The area of inhalation toxicology was considered to be of such importance that a new program, at least new to our pesticide laboratory, has been generated and has been divided into five phases. These five phases are, briefly, generation of a respirable particle, chemical analysis of the chamber content, acute toxicology, gross and microscopic pathology of selected tissues, and clinical chemistry.

The first phase of the work includes the generation of respirable particles in the general range of 1- to 3-micron size; this is a very artifical figure and has only a small relation to the pesticide size range obtained in agricultural use. Significant questions have been raised within the framework of this effort as to the significance of the work other than on the basis of a toxicological evaluation and not an environmental or a use pattern evaluation.

The use of a highly respirable particle, although artificial with regard to use in agriculture, will be of value in the initial phases of this effort. Toxicity studies will be done to compare the oral, dermal, systemic, and inhalation routes of administration of some of these materials to rats. Inhalation studies would include 1-hour or 4-hour exposures. It has generally been considered in the framework of this work that we would anticipate lower toxicity values for the inhalation route, and the significance of these values would be evaluated and future studies conducted to determine their actual worth.

At the present time we can only call them reference materials. Gross and microscopic pathology will be carried out routinely on lungs, with additional histological examination on selected tissues when such study is considered valuable. The clinical chemistry analysis will include analysis of liver, kidney, lung, blood, and various other tissues for the presence of pesticide, not classical clinical chemistry. We've called it clinical chemistry. It is actually analytical chemistry for pesticide residues in the body.

It is anticipated that this program would allow EPA to utilize inhalation capability as a part of the toxicological assessment of what we're now considering to be substitute chemicals. I would like to get across a major thought: Our laboratory exists for two purposes. These purposes are to do research in the particular areas that we find need research and are of interest to the regulatory arm of our Agency in Washington, and to directly respond, to fill out our data base as deemed necessary by the C&E Division in its reviews.

LONG-RANGE HEALTH EFFECTS

John L. Buckley, Ph. D*

I've already said in a couple of different sessions here what I thought the needs and goals of EPA research in relation to health and pesticides were, and I simply wish to reiterate those very briefly.

Predominantly it's a matter of methods development, and the part that I'm particularly concerned with now is methods development that will be quicker, better, and cheaper, that will let us know with a greater degree of assurance at an earlier time what effects occur in man as a result of a particular exposure. The areas I wish to emphasize are the long-term, low-dose aspects — carcinogenesis, mutagenesis, in particular, and to some extent teratogenesis.

I think we probably would all agree that in the area of mutagenesis — and I heard this expressed more cogently and clearly by others — we don't have a good method. Each individual who carries out a particular method will defend that up to a point, but the fact is he's not all that certain when he gets through how you interpret his results in relation to man, and that's where the question really is. We're kind of fumbling around in the dark along with, I must say, the rest of the scientific community. We're prepared to support work, some of which will almost certainly not pay off, but we think that comparative studies and attempts in different ways and support of sometimes far out ideas may well be useful in this area. From this we hope eventually to contribute to better methods of assessing effects of chemicals in general, and in this case perhaps specifically.

As to other activities that we have, I picked out carcinogenesis, and again I don't want to step on the toes of NCI or other groups concerned predominantly

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*Acting Deputy Administrator for Program Integration, U. S. Environmental Protection Agency

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with this area. But all of you who are in the chemical business know better than I that this is a magic word, that if it's associated with a compound, it's pretty close to a death knell for the compound.

We've got quite a lot of information on tumor formation in various and sundry animals, but we do have a big problem in extrapolation of animal data to man. Here again, as in mutagenesis, we'd like to improve our abilities to extrapolate in this area. We really are not all that interested in tumor rates in rats or mice or monkeys for that matter, and I'll make an observation as an ex-wildlife manager, that I'm not even that much interested in it in most kinds of wild animals, simply because few animals in a wild population live long enough for anything of this sort to be significant in terms of the population.

So whatever we do in terms of carcinogenesis, even though we do it on other organisms, we are really doing in order to understand probabilities of these kinds of effects in man. Now you can fault us, perhaps, on the contracts that we let, the interagency transfers that we have, or the research that we ourselves carry out, but you cannot fault us, I believe, on the goals that we have in trying to support this kind of research. This research is to enable us to make better judgments than we can now on whether the substance of interest, whatever it may be, causes in man the effects that we are looking for.

That really is what the game is. As a population biologist and not as a human health specialist, it's with some temerity that I stand before a group such as this and speak to the topic of human health, and for that reason if for no other I'd like to wrap it up there as far as comments on human health.

DR. AXELROD: So often expressed from the podium," I have a compulsion coming on," and it relates to some of the things that John said, all of which I agree with, but I would make a more or less philosophical expression of trepidation at this point, and that relates to the place of the scientist in the American society — things that Phil Handler at the Academy had discussed and others. And I think it's important that the scientist take his proper place in our society, and that there is in the vernacular no "cop-out" for expressing his concerns and his data banks in any process, and law, and any regulation that impacts on himself as a human being and as a scientist in general, so I'm sure that John and I both agree that the scientist in EPA has a proper place in the decision-making process.

DR. BUCKLEY: Yes, Len and I have talked about this over lunch and no doubt we will talk about it back at the office too. The only point that I feel very strongly about and I've already expressed is that there are some things where scientists should feel prepared to stand and beat on the table and say "this is the way things are."

But to the extent of saying we should do something because of that information, I think that's a very difficult step that we all wish to weigh. Here I will demand my right to a vote as a member of society, but I'll try and refrain from imposing my scientific views and confusing those with my social views. Are there questions either of Ron or of myself?

MR. JOHN J. HOOD: I have a question for Dr. Baron. Following his so-called quick and dirty review of these various technical materials for contaminants and/or impurities, what will be the criteria that will be followed for further scrutiny of these materials?

DR. RONALD BARON: We've made up some arbitrary numbers to go along with our quick and dirty study as to how much further we will go after we've done our quick and dirty study. For anything that would be present in a level of .05 percent and above it would be considered of value to know what the compound is and what the identity of the material is. If on identifying the material or if on the basis of the paper evaluation, the material is thought to have some toxicological properties that we're interested in, we will go further in that respect.

If the material is present at a level of .1 percent in the technical mixture, we will probably make a considerable effort to get the material identified. We may not go any further than GC mass spec and the computer analysis of the peaks, but we will make an effort to identify materials at .1 percent; .05 percent is sort of a flag.

DR. R. E. HANSON: When you talk about quick and dirty and in the same breath you talk about levels of 0.05 percent, I just don't believe you can talk quick and dirty. A total analysis of some of these compounds would cost you in the terms of 1 to 2 man-years or more, and I know, we've spent it. And yet you're going to look at levels at .05 percent of compounds you don't even know are there. I just can't seem to understand what you're talking about quick and dirty with what I know about total analysis of pesticides and contaminants at the .05 level.

DR. BARON: It's an interesting statement you just made. I don't hear a question in it, but I would like to respond to your statement in that I agree with you totally. The quick and dirty approach to this is a reflection on two things. One, for the major thrust of our research program in all aspects of research we want to know what we're working with, so we are planning on putting these materials which are capable of being put through the GC with a mass spec and a computer analysis of the peaks that come out to determine quickly what is there, and if the material shows up on a chart paper as being a contamination and if it looks like it could be part of that which we're interested in, then that peak would then go through the mass spec. We'd then come up with a series of potential compounds that it could be.

This is not going to be a major undertaking with all the pesticides in our programs. It's obvious that it cannot be. I want to point out that it can be a quick and dirty. I don't really think that there's going to be a major thrust to identify or to pull out and try to identify all of the small pieces of technical mixtures.

DR. BUCKLEY: I, as a nonchemist, have no right to speak to the details of this. I have, however, been associated with investigations of various and sundry pesticides long enough to know that invariably there are questions as to whether it's the technical material, the intended active ingredient, or just what that causes some observed effect. I think the question of trying to sort this out is real. I think the point of knowing, to the extent you can, the makeup of the substance being toxicologically or environmentally or otherwise investigated is clearly worthwhile. I think all of us can think of horror stories where we've used different substances and ended up with contradictory results.

You may well fault us on the details of what we tell you we want to do. We will certainly solicit your advice on how we should do some of this. I would make one further point, that in my view, the place we start is asking you to tell us, as clearly as you can and as far as you're willing to, the makeup of the product which you provide us. It seems to me that for us this is really the most important starting point.

There is a matter of timing and sequence here. If we were to look through all pesticidal chemicals, looking for what the contaminants are or what the ingredients are or what the average composition is or things of this sort, we have in front of us an endless chore. If we do have a particular question on a compound, in the sense that we see an observed effect which either is inconsistent with what we would have expected to be the case, knowing something of structure and function in related compounds and so on, or if for other reasons it seems important to look at this, as was the case with the dioxins in 2,4,5-T, then I believe we ought to do it. I have nothing further to say on the topic, but I don't intend to close off discussion at that point.

DR. JOHN McCARTHY: Ron, as I understood your description of the inhalation program, it was to determine the acute LC 50 of materials that needed such information. Are there other plans beyond that based on results from those tests?

DR. BARON: At this particular point in time, we are finding our way as to what we're going to do. We have two major areas of pesticide inhalation research programmed, but they don't relate to what we are going to do with the acute toxicity data.

The two other areas that are being considered for further work are utilizing inhalation — and I'd like to reemphasize that we consider inhalation to be another means of entry, not the same in quality, but just as oral or dermal, it is another mode of administering a compound for metabolism studies — and we are planning to give some serious consideration of this question of particle size distribution in actual life and how our studies on a very respirable particle relate to what we can consider to be an agricultural or a problem in actual use.

So these two particular areas of particle size, distribution and effect, and metabolism — and because we do have a very good reproductive physiology group at Research Triangle Part, we will probably be going into reproductive physiology as affected by inhalation as a route of administration. I hope that answers some of your questions. I know I walked around your question very nicely. I can't really put my finger on what we're going to do with the data when we compare these four routes as I've said. This is our feeling process at this point.

DR. JERRY SMITH: One statement and one question. The emphasis was given on development of new methodology and trying to come up with short and quicker ways of assessing toxicity hazards. In this area are we not getting to the point where we are duplicating some of the efforts of NCTR? In addition, I would encourage us not to do method development on unknown materials that are under evaluation but to do our method development on materials about which we know the most. The question relates to the statement yesterday that we should do more of our studies knowing what the effect of the materials are in man. Do you have any intentions or any plans for doing metabolic studies or other work in man with pesticides under consideration, so that more appropriate experimental animals can be selected for these studies?

DR. BUCKLEY: I'd rather respond to your statement than your question. It is not our intent to duplicate anything at NCTR. In fact some of the funds that we're talking about are used at NCTR, and they in fact are a supplement to that program. I have no intent from my point of view of seeking a broadening or duplication of effort here. I'm sorry that Morris Cranmer is not here today. I guess we didn't arrange things very well that way, but he could have answered that or commented on the statement somewhat more precisely.

As to the studies in man, I think it's probably fair to say that at this juncture in time I know of no plans, no arrangement for volunteers or otherwise, nothing definite. Neither do I rule out the possibility or the desirability of doing this. I think probably many of you here are much more aware than I of the parts of the world in which one now does human studies, and the things which lead to this, and I would rather not comment further on that.

Nonetheless, I do want to make the point that the effect on man, or the lack of effect on man preferably, is the goal of this whole set of things that we are talking about right now. I'm sure that I've evaded the question rather than answered, but it's the closest I can come right now.

QUESTION: You have at Research Triangle a health effects group under John Knelson. You also have inhalation work going on at the NIEHS. Are you tied in with these groups or is this a separate group?

DR. BUCKLEY: The group under Dr. Knelson is a different labotatory in the same research center under the same overall leadership, and the answer then is yes, we are closely tied in. The answer at NIEHS is that we have free and frequent exchange among people at all levels. When we have meetings planning work in relation to any topic at Research Triangle Park, I think it's fair to say that the people from Dr. Rall's staff participate with us and we with them. My personal biases are that you have the work that you need done in the most appropriate place that you're able to find. I feel no compulsion to see that EPA has all the talents that it needs to do everything it might be asked to do in-house.

So, the short answer is that we're not trying to take over all the research in the world. We are trying to fill in some rather explicit gaps which now exist. We are trying to support other people in doing things which we find are worthwhile, and we hope that we buy the most with the taxpayers' dollar in the process of doing this.

DR. GORDON NEWELL: I've heard several comments during this meeting about the relevance of our studies as they apply to man; certainly many of my biochemist friends here know that today we can use fresh human liver (from necropsy cases) to conduct preliminary metabolism studies on compounds of concern. We can identify the human in vitro metabolites and then study the compound in various animal species; in certain laboratories this is a regular practice. Although this approach is not as satisfactory as using the whole animal, at least it gets you one step closer to man. Studies with drugs often are concerned with efficacy, but here we're concerned with safety. Through the comparative metabolism approach we now can obtain a more realistic understanding of a compound than we could a few years ago.

DR. BUCKLEY: I think other points of the same sort, of course, are in comparative pharmacology, comparative physiology, and comparative metabolism. The points and questions that have been raised that the animal model reflects systems of responses of interest in man deserve much more attention in selection than has been given in the past.

QUESTION: I didn't see any reference at all in your health effects work relating to epidemiological estimation of cause and effect relationships on populations, possibly international comparisons and that sort of thing. I know the Office of Pesticides has the function in the technical services division, but it occurs to me that maybe some of this type of work could be addressed by you also in relation to this program.

DR. BUCKLEY: It's difficult to respond to this in a nonbureaucractic way, and the only point that I would like to make is that the proof of the pudding is in the eating, as it were, and to the degree that one can look at what really does happen in the world in terms of man, this is clearly the most satisfying thing that you can do. I personally think that there are a number of epidemiological opportunities that have not yet been adequately exploited — not all of them in this country. Either with funds associated with this program or with other funds, it is our intent to try and exploit some of those — exploit in the sense of invest resources in them.

You know, without saying that we will do research on the following things or support epidemiology, I would submit that there are parts of the world where certain kinds of chemicals are used and the exposure levels are considerably higher than they are in other circumstances, and the populations at risk are sufficiently large that one may be able to observe effects if present where one cannot observe them in relatively small numbers.

There are, you know, many ins and outs of this, and I would hope that we can exploit this source of information. On the other hand, there are some other kinds of epidemiology in a sense that trouble me. Some of the cohorts of people available for study are relatively so small that the expectation of whatever event is searched for is not likely to show up. The infrequency of things just sort of beats you, and so there are many things that one would like to do epidmiologically which really are not practical that way.

Now, someplace between this rather negative view that says if you can't find out what you want to know, don't bother doing it, and on the other hand saying that man is the only final proof of this and if you don't see it in man you can't believe it, it does seem to me that there are some real and important opportunities for epidemiological work which ought to be and I hope will be carried out.

DR. R. E. HANSON: I think part of industry's concern has been that we know there are compounds picked for the program, we have been requested for technical material, yet the people that are requesting the material do not seem to have any data case in front of them. I would like to know who we present the data base case to, number one the data that's already within the files, and second, any new data that we have in our own files that has not been transmitted forward, but I think we get an impression that you're working in a vacuum.

And yet you're telling me you want us to come to you. Well, we're happy to come to you, but who are we coming to? Are we coming to Len, to John, or to both? I think this is part of my apprehension, because we know one of our compounds is picked. We've been asked for the technical product. Yet we haven't the foggiest notion what you're really going to do, who is telling you what to do, and what kind of base case you already have in front of you that says I shouldn't do this, this, and this, because it's already been done.

I look down through your whole list, and for the particular compound I'm thinking about if you use the classical techniques that are already there, I have to say it's already been done, and this I think is the little funny feelings I get about what's going on with the program is you seem to work for the same Agency, but then I'm not sure.

DR. BUCKLEY: Well, may I suggest that the communication between us and you has been less than adequate, and may I hint that perhaps the communication between those of us inside EPA may, in fact, have been less than adequate. May I suggest that we're working reasonably hard at fixing this. We'd like to share more openly with you than we have.

We want to share with you what it is that we want to do and why we want to do it. From my perspective, we'd like your advice and assistance. For you to tell us that our plans are stupid won't hurt my feelings in any way, and for you to tell me that you already have this information and we are welcome to it, will certainly please me.

Now, as to the first part of your question, whether you should address it to me or to Dr. Axelrod, I think probably it really should be to Len, because our understanding on this in a general way up until now has been that the contacts with industry were initially largely to be through his office rather than mine. I think that with that having been done, and it has, I would think that the time has come for closer exchanges and particularly at the technical detail level between my people and yours.

And the point I want to make here is that I'm troubled a little bit because I can conceive of 25 or so different individuals dealing with different parts of this program in my organization coming and asking for essentially the same kind of thing. We had thought that would be annoying to you and we've tried to turn it off. On the other hand, there is the fact that the person who wants something is likely to tell you with more precision why he wants it and lay at rest any questions there may be about it than the other way around. We are in fact trying to arrange so that we will set up a first set of contacts, which then may broaden so that the kinds of questions and kinds of comments that you make now will be adequately addressed.

As far as requests to you for compounds, it's our intent that this be through Dr. Baron, and if there are detailed questions beyond that we'd like to take it up and pursue it. I'm sorry for the disruption and confusion which obviously has arisen in this program, and the reason that we asked Ron to say some of the things that he did, to include this explicitly in his presentation this morning, was to try and get out for public discussion and clarification what it was we were about and why.

And if the details don't satisfy you, in the way in which it has been explained and discussed, then I would like to pursue this further, because I see no gain in having mistrust, worry, and discomfort on the part of any of you or of us.

DR. KORP: I just wanted to say how really pleased I was to be here all three days of this meeting. I've heard a great deal, I've learned a great deal, I'm very appreciative. The suggestions were fine.

We will take advantage of all your suggestions. We will pay attention to them, those where we can find something reasonable and feasible, we will implement improvements in this program and in our programs. I look forward to seeing you all again at some meeting at Washington headquarters or at your companies. I thank you very, very much.

DR. AXELROD: I'm not quite sure if I understood everything John was saying, but you've got to understand as we put our cards on the table, this program was impacted on us very, very quickly, and it's really only recently that there have been many clarifications in the thrust of the program and its implementation. I think where some of the confusion lay was that one area was a "review concept," the other was "research" to be carried out by ORD in the various geographic locations.

I think that what was discussed this morning really related to something that was to be and is to be implemented at the research level, and that was studies of some of the impurities in some of the compounds. In that respect let me say that not all syntheses would or could lead to the types of impurities that John was talking about for further study, so that we're not cutting across all. If a particular synthesis could lead to an obvious problem of toxicological effects, then those specific compounds would be studied.

It was confusing because as someone once said, "Throw a pencil, throw a fit, but throw something," and we had to get this program going for many obvious and some perhaps not too obvious reasons. I think that the communication lines were very clearly delineated henceforth. I think that the one place where there was a question was in who do you go to for what, who's asking for what, and why are you asking for it.

I think that just at the level of strict interpersonal relations, everyone is entitled to know in writing why something is wanted. I think that in the review areas — and we've had very good fortune in this area — there has been a good liaison developed, so that in the particular compound of our interest, a number of companies have come forth with their data bases. And at least in one case the data was much more than we could retrieve from the literature or from our data banks and registration, and it became obvious that certain aspects of further study would not be necessary, because there was more data that was brought to us from the company than we could possibly achieve from outside information sources.

I think that all of you in industry who have some trepidation left concerning the flow of information systems will be satisfied by a rather rigorous and concerted effort to delineate point for point who's on first and who's on second. And hopefully, we're all on home base, so that you all get letters that say "For this piece of the action please address your comments to X, Y, and Z or preferably just to X. I think what John said about too many people, "too many cooks spoiling the broth" is very appropriate.

We have two or at a maximum three points for data retrieving and for contact, depending on where the thrust is. Obviously, we want to minimize the number of letters, the number of round robins and information retrievals, and certainly the trepidation that goes with all of that, because of wasted time and wasted effort.

In the areas of the basic research in John's operation, there would be obviously a contact point for the type of thing that was wanted, i.e., a certain amount of compounds. Where there is the review process it would be sent to a headquarters contact point, perhaps in our office, for getting back a package, but if you all paid attention to that schematic placed on the screen yesterday by Ken Olsen, you would see that in the proper way, in the best of systems, before anything happens, the corporation is contacted. We sit down and at that point decide what we want, from whom we want it, and for what we want it.

DR. BUCKLEY: I have a few observations that I think will not take more than a couple of minutes. They're a reiteration of things I've said several times. First, I feel very strongly that it's important to ask the right questions in a research frame, and the right questions involve dealing with the world as it really is, and not a kind of a hypothetical world. Associated with this, is the question of the significance of any observable fact. The answer to the question "so what?"

I think we've seen at this meeting, some evidence of misinterpretation of information, and we've also seen some information which is undoubtedly accurate, but wholly irrelevant. In other terms, this is sometimes thought of as a red herring, and this area of interest is no more devoid of red herrings than most other fields.

It does seem to me that the phraseology of the question to be investigated is really important. I think of a point outside of the pesticide field that I would use to illustrate this. At a meeting in Athens, Georgia, some months back a man was explaining that in a small test tube system he was using, he had demonstrated that bacteria were able, with materials that occur in the environment, to produce nitrosamines. I began to pursue the question in somewhat more detail to determine the conditions that prevailed — temperature, pH, concentrations, etc.

It's not a question of "could it?" The question is, in the world as it is, "does it?" The point I want to make is that we haven't always been very careful in the questions that we've asked, and we haven't always made the best possible interpretation of the significance of what we've found. The major of Jim Hill's presentation here this morning, which in my view was one of the highlights, is the capability of putting it all together, of putting things in their proper perspective, of evaluating the relative importance of various events and observable facts.

We'll continue to work on this kind of a framework, and we earnestly solicit your contributions of knowledge and data that we can use in these kinds of interpretations.

I'd like to close simply by saying that when I came to this meeting I felt somewhat as though I were walking into a miasma of suspicion, but I leave with a very much better feeling than that I arrived with. I would hope that our cooperation can increase in productiveness for us and for you, and that we won't let suspicions that arise "pressure cook" until they become unbearable. I'll bring mine to you if you'll bring yours to me. Thank you all.

END OF PROCEEDINGS

APPENDIX I
Agenda

epa symposium

alternative chemicals program

with an overview of

pesticide research & development

STOUFFER'S DENVER INN

DENVER, COLORADO

August 14 - 16, 1974

EPA SYMPOSIUM

Alternative Chemicals Program
With an Overview of
Pesticide Research and Development

OBJECTIVES

- To acquaint the pesticide industry and academia with the Alternative Chemicals Program and its review processes.
- To present the status of the EPA Alternative Chemicals Program and pesticide research and development activities.
- To provide an overview of U.S. and world-wide pesticide research and development

TUESDAY, AUGUST 13, 1974

7:30 - 9:00 p.m. Conference Registration
Convention Corridor

WEDNESDAY, AUGUST 14, 1974

Alternative Chemicals Program Organization and Review Processes

Dr. Henry J. Korp, Moderator
South Ballroom

8:15 Late Registration

9:15 Welcome and Introduction
Functions and Overview of the
Office of Pesticide Programs:
Highlights of OPP Programs
Dr. Henry J. Korp

10:00 The Alternative Chemicals Program:
Purpose, Organization, Operation
Dr. Leonard R. Axelrod

10:30 BREAK

10:45 The Alternative Chemicals Program:
Flow Charts and Key Decision Points
Mr. Kenneth O. Olsen

11:15 OPP Liaison
Dr. Frederick W. Whittemore

11:45 BUFFET — Central Ballroom

1:00 Panel Presentations and Discussions
Dr. Leonard R. Axelrod,
Moderator

General Description of the Initial
Scientific and Mini Economic Review
Process
Dr. Thomas D. Burkhalter
Mr. Jeff Conopask

General Description of the Full
Biosphere and Socioeconomic
Reviews Process
Dr. Lamar B. Dale
Dr. Arnold L. Aspelin

3:00 BREAK

3:15 Progress in EPA Research:
New Directions and Overview
Dr. John L. Buckley

6:00 RECEPTION — Buckingham

7:00 DINNER — Buckingham
Towards a New Perspective on
Pesticides
Dr. Henry J. Korp

THURSDAY, AUGUST 15, 1974

Overview of Worldwide Pesticide Research

Dr. Morris Cranmer, Moderator
South Ballroom

9:15 Worldwide Perspectives of Pesticide Research
Dr. Frederick Coulston

9:45 The Role of WHO in Pesticide Research
Dr. Frank C. Lu

10:15 The Role of FAO in Pesticide Research
Dr. Edgar E. Turtle

10:45 BREAK

11:00 U. S. Participation in CODEX
Mr. Lowell L. Miller

11:30 International Topic
Prof. Radojica Klajic

12:00 LUNCH — Central Ballroom
Regional Role in Pesticide Programs
Mr. Robert Harding*

1:30 National Environmental Pesticide Monitoring Program
Dr. William Murray

2:00 What the USDA Does in Pesticide Research
Dr. Phillip Kearney*

2:30 What the USDI Does in Pesticide Research
Mr. Jerry Longcore

3:00 BREAK

3:15 From Industrial R & D to the Marketplace
Dr. Edwin F. Alder

3:45 Research and Special Considerations: Nonagricultural Use Pesticides
Mr. Melvin Garbett

4:15 The Future of Pesticide Research: A Challenge
Dr. Leonard R. Axelrod

*Speeches not available for publication

FRIDAY, AUGUST 16, 1974

Pesticides Research in the Environmental Protection Agency

Dr. John L. Buckley, Moderator
South Ballroom

8:30 Introduction
Dr. John L. Buckley

Ecological Effects

8:45 Overview
Dr. Norman Glass

8:50 Terrestrial Effects
Dr. James Gillett

9:15 Marine Effects
Dr. Thomas Duke

9:40 Fresh Water Effects
Mr. John Eaton

10:05 Fresh Water Transport Processes
Mr. James Hill

10:30 Question and Answer Period

10:55 BREAK

Human Health Aspects

11:10 Intra- and Extramural Health Effects Research
Dr. Ronald Baron

11:40 Long-Range Health Effects
Dr. John L. Buckley

12:10 Question and Answer Period

12:40 ADJOURNMENT

APPENDIX II

Participants

Mike Adair
The Ansul Co.

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Vice President, Lilly Research Laboratories

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Robert B. Foster
House Appropriations Committee

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Environmental Advisor
O. M. Scott & Sons

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Chemical Specialties Manufacturers Association, representative

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